TRANSACTIONS

OF THE

AMERICAN PEDIATRIC SOCIETY

TWENTY-FOURTH SESSION

HELD AT THE HOMESTEAD HOTEL, HOT SPRINGS, VIRGINIA
MAY 29, 30 AND 31, 1912

EDITED BY
LINNAEUS EDFORD LA FÉTRA, M.D.

VOLUME XXIV.

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CHICAGO

CONTENTS

PRESIDENTS

1889. A. Jacobi, M.D.
1890. J. Lewis Smith, M.D.
1891. T. M. Rotch, M.D.
1892. Wm. Osler, M.D.
1893. A. D. Blackader, M.D.
1894. John M. Keating, M.D.
1895. F. Forchheimer, M.D.
1896. Joseph O'Dwyer, M.D.
1897. Samuel S. Adams, M.D.
1898. L. Emmett Holt, M.D.
1899. Wm. P. Northrup, M.D.
1900. Henry Koplik, M.D.
1901. Wm. D. Booker, M.D.
1902. W. S. Christopher, M.D.
1903. J. P. Crozer Griffith, M.D.
1904. Augustus Caillé, M.D.
1905. C. G. Jennings, M.D.
1906. A. Jacobi, M.D.
1907. B. K. Rachford, M.D.
1908. C. G. Kerley, M.D.
1909. Charles P. Putnam, M.D.
1910. David L. Edsall, M.D.
1911. Henry Dwight Chapin, M.D.
1912. Walter Lester Carr, M.D.
1913. John Lovett Morse, M.D.

OFFICERS, 1912

President ..... Walter Lester Carr, M.D.
Vice-President ..... Percival J. Eaton, M.D.
Secretary ..... Samuel S. Adams, M.D.
Treasurer ..... Chas. Hunter Dunn, M.D.
Recorder and Editor ..... L. E. La Fétra, M.D.

COUNCIL

S. McC. Hamill, M.D., *Chairman*

Geo. N. Acker, M.D.
R. G. Freeman, M.D.
Alfred Hand, Jr., M.D.
L. E. La Fétra, M.D.
Isaac A. Abt., M.D.
John Howland, M.D.

MEETING PLACES

1888. Washington, D. C. (Organization), September 18.
1889. Washington and Baltimore, September 20 and 21.
1890. New York, June 3 and 4.
1891. Washington, September 22 and 25.
1892. Boston, May 2, 3 and 4.
1893. West Point, N. Y., May 24, 25 and 26.
1894. Washington, May 29 and June 1.
1895. Virginia Hot Springs, May 27, 28 and 29.
1896. Montreal, May 25, 26 and 27.
1897. Washington, May 4, 5 and 6.
1898. Cincinnati, June 1, 2 and 3.
1899. Deer Park, June 27, 28 and 29.
1900. Washington, May 1, 2 and 3.
1901. Niagara Falls, May 27, 28 and 29.
1902. Boston, May 26, 27 and 28.
1903. Washington, May 12, 13 and 14.
1904. Detroit, May 30, 31 and June 1.
1905. Lake George, N. Y., June 19, 20 and 21.
1906. Atlantic City, N. J., May 30, 31 and June 1.
1907. Washington, May 7, 8 and 9.

1908. Delaware Water Gap, May 25, 26 and 27.
1909. Lenox, Mass., May 27 and 28.
1910. Washington, May 3, 4 and 5.
1911. Lake Mohonk, N. Y., May 31 and June 1 and 2.
1912. Hot Springs, Va., May 29, 30 and 31.
1913. Washington, May 5, 6 and 7.

OFFICERS, 1913

President ..... J. Lovett Morse, M.D.
Vice-President ..... John Ruhräh, M.D.
Secretary ..... Samuel S. Adams, M.D.
Treasurer ..... Chas. Hunter Dunn, M.D.
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Isaac A. Abt., M.D.
John Howland, M.D.
Thomas Morgan Rotch, M.D.

MEMBERS

1903. Abt., Isaac A., M.D. ..... 4326 Vincennes Avenue, Chicago
1893. Acker, George N., M.D. ..... 913 Sixteenth Street, Washington
O Adams, Samuel S., M.D. ..... 1 Dupont Circle, Washington
1894. Baines, Allen M., M.D. ..... 228 Bloor Street, Toronto
C Blackader, A. D., M.D. ..... 236 Mountain Street, Montreal
1907. Bovaird David, Jr., M.D. ..... 137 East Sixtieth Street, New York
1911. Bowditch, Henry I., M.D. ..... 416 Marlborough Street, Boston
1911. Butterworth, William W., M.D. ..... New Orleans, La.
O Caillé, Augustus, M.D. ..... 753 Madison Avenue, New York
1911. Carpenter, Howard C., M.D. ..... 1805 Spruce Street, Philadelphia
O Carr, Walter Lester, M.D. ..... 68 West Fifty-First Street, New York
O Chapin, Henry Dwight, M.D. ..... 51 West Fifty-First Street, New York
1897. Churchill, F. S., M.D. ..... 1259 North State Street, Chicago
1910. Coit, Henry L., M.D. ..... 277 Mt. Prospect Avenue, Newark, N. J.
1898. Cotton, A. C., M.D. ..... 1485 Jackson Boulevard, Chicago
1909. Cowie, D. M., M.D. ..... Lawrence Building, Ann Arbor, Mich.
1892. Crandall, Floyd M., M.D. ..... 113 West Ninety-Fifth Street, New York
O Dorning, John, M.D. ..... 124 West Eighty-First Street, New York
1906. Dunn, Charles Hunter, M.D. ..... 220 Marlborough Street, Boston
1904. Eaton, Percival J., M.D. ..... 131 N. Highland Avenue, E. E., Pittsburgh
1902. Edsall, David L., M.D. ..... 1432 Pine Street, Philadelphia
1907. Fife, Charles A., M.D. ..... 1927 Chestnut Street, Philadelphia
O Forcheimer, F., M.D. ..... Fourth and Sycamore Streets, Cincinnati
1895. Freeman, Rowland G., M.D. ..... 211 West Fifty-Seventh Street, New York
1910. Gittings, J. C., M.D. ..... 3492 Chestnut Street, Philadelphia
1897. Graham, E. E., M.D. ..... 1713 Spruce Street, Philadelphia
1892. Griffith, J. P. Crozer, M.D. ..... 1810 Spruce Street, Philadelphia
1898. Hamill, S. McC., M.D. ..... 1822 Spruce Street, Philadelphia
1902. Hand, Alfred, Jr., M.D. ..... 1724 Pine Street, Philadelphia
1910. Haynes, Royal S., M.D. ..... New York
1909. Heiman, Henry, M.D. ..... 20 West Eighty-Eighth Street, New York

1910. Herrman, Charles, M.D. .....250 West Eighty-Eighth Street, New York
O Holt, L. Emmett, M.D. .....14 West Fifty-Fifth Street, New York
1905. Howland, John, M.D. .....
O Huber, F., M.D. .....209 East Seventeenth Street, New York
O Jacobi, A., M.D. .....19 East Forty-Seventh Street, New York
1894. Jennings, Charles G., M.D. .....457 Jefferson Avenue, Detroit
1896. Kerley, Charles G., M.D. .....132 West Eighty-First Street, New York
1905. Knox, J. H. Mason, M.D. .....804 Cathedral Street, Baltimore
O Koplik, Henry, M.D. .....30 East Sixty-Second Street, New York
1903. Ladd, Maynard, M.D. .....270 Clarendon Street, Boston
1903. La Fétra, Linnæus E., M.D. .....113 East Sixty-First Street, New York
1911. Lucas, William Palmer, M.D. .....261 Beacon Street, Boston
1912. McLanahan, H. M., M.D. .....468 Brandeis Building, Omaha
1909. Machell, H. T., M.D. .....95 Bellevue Avenue, Toronto
1907. Meara, Frank S., M.D. .....400 West End Avenue, New York
1898. Miller, D. J. Milton, M.D. ....127 S. Illinois Avenue, Atlantic City, N. J.
1896. Morse, J. Lovett, M.D. .....70 Bay State Road, Boston
1908. Nicoll, Matthias, M.D. .....124 East Sixtieth Street, New York
O Northrup, William P., M.D. ....57 East Seventy-Ninth Street, New York
1910. Pisek, Godfrey R., M.D. .....36 East Sixty-Second Street, New York
1912. Porter, R. Langley, M.D. .....240 Stockton Street, San Francisco
O Putnam, Charles P., M.D. .....63 Marlborough Street, Boston
1894. Rachford, B. K., M.D. .....323 Broadway, Cincinnati
O Rotch, Thomas Morgan, M.D. .....197 Commonwealth Avenue, Boston
1905. Ruhräh, John, M.D. .....839 North Eutaw Street, Baltimore
1900. Saunders, E. W., M.D. .....3003 Lafayette Avenue St. Louis, Mo.
1912. Schloss, Oscar M., M.D. .....54 W. One Hundred Fourth St., New York
1902. Shaw, Henry L. K., M.D. .....361 State Street, Albany
1891. Snow, Irving M., M.D. .....476 Franklin Street, Buffalo
1905. Southworth, Thomas S., M.D. .....807 Madison Avenue, New York
O Starr, Louis, M.D. .....1818 South Rittenhouse Square, Philadelphia
1911. Talbot, Fritz B., M.D. .....311 Beacon Street, Boston
1910. Tileston, Wilder, M.D. .....424 Temple Street, New Haven
1889. Townsend, Charles W., M.D. .....76 Marlborough Street, Boston
1912. Veeder, Borden S., M.D. .....1806 Locust Street, St. Louis, Mo.
1895. Wentworth, A. H., M.D. .....352 Marlborough Street, Boston
1896. Westcott, Thompson S., M.D. .....1720 Pine Street, Philadelphia
1897. Williams, Harold, M.D. .....528 Beacon Street, Boston
O Winters, J. E., M.D. .....25 West Thirty-Seventh Street, New York

Note.—The first column gives the date of election to the Society. The organizers of the Society are designated by "O," the date being 1888.

HONORARY MEMBERS

Dr. John Thompson ..... Edinburgh, Scotland
Dr. George F. Still .....London, England
Dr. O. Heubner ..... Berlin, Germany
Dr. William Osler ..... Oxford, England
Dr. A. Baginsky ..... Berlin, Germany
Dr. V. Hutinel ..... Paris, France
Dr. Charles Rauchfuss .....St. Petersburg, Russia

Deceased

JOHN A. JEFFRIES, M.D.
Born, September 2, 1859.
Died, March 26, 1892.

THOMAS F. SHERMAN, M.D.
Born, March 17, 1856.
Died, September 26, 1893.

JOHN M. KEATING, M.D.
Born, April 20, 1852,
Died, November 17, 1893.

CHARLES WARRINGTON EARLE, M.D.
Born, 1845,
Died, November 19, 1893.

J. LEWIS SMITH, M.D.
Born, October 15, 1827,
Died, June 9, 1897.

JOSEPH O'DWYER, M.D.
Born, October 12, 1841,
Died, January 7, 1898.

JOHN HENRY FRUITNIGHT, M.D.
Born, November 9, 1851,
Died, December 18, 1900.

FREDERICK A. PACKARD, M.D.
Born, November 17, 1862.
Died, November 1, 1902.

WALTER S. CHRISTOPHER, M.D.
Born, 1859,
Died, March 2, 1905.

LEROY MILTON YALE, M.D.
Born, February 12, 1841,
Died, September 12, 1906.

JAMES PARK WEST, M.D.
Born, June 27, 1858,
Died, June 25, 1908.

CONSTITUTION AND BY-LAWS OF THE AMERICAN PEDIATRIC SOCIETY

ARTICLE I

Name and Object of the Society

The Society shall be known as the American Pediatric Society, and shall hold an annual meeting.

It has for its object the advancement of the knowledge of physiology, pathology, and therapeutics of infancy and childhood.

ARTICLE II

Proceedings

The proceedings shall consist of:

1. Discussions on subjects previously selected.
2. Original communications.
3. Demonstrations of gross and microscopic preparations, apparatus, and instruments.

ARTICLE III

Members

The Society shall be composed of two classes of members to be designated: (1) active members and (2) honorary members.

The number of active members shall be limited to seventy-five.

The number of honorary members shall be limited to twenty-five.

ARTICLE IV

Election of Active Members

Nominations to membership, signed by two members of the Society, must be made in writing at least one meeting prior to election.

Nominations should be made to the Secretary, whose duty it shall be to require the nominators to write a personal letter endorsing and stating the qualifications of the nominee, and at the same time furnishing a list of the nominee's professional position and publications, with reprints of the latter, when obtainable.

It shall be the duty of the Secretary to transmit to the chairman of the council all the above papers pertaining to each nominee, at least three months prior to his possible election.*

*In the event that required information relating to candidates for membership is not furnished to the Secretary by three months before the time of the meeting at which they would be considered, such candidates for election shall be held over for another year. (Resolution adopted 1912.)

The chairman of the council shall transmit the above named papers to the other members of the council in the order of their seniority as council members, the junior member of the council returning them to the Secretary.

It shall also be the duty of the Secretary to furnish a printed list of all nominees at least once a year to every member of the Society, and it shall be the duty of the members of the Society, without solicitation, to furnish the council with any information that they may possess as to the fitness of the nominees to become members of the Society.

Upon nomination by the council, members shall be elected by the Society by ballot. A two-thirds vote of the members present shall be necessary for election.

ARTICLE V

Election of Honorary Members

Physicians of sufficient eminence to merit the distinction may be elected honorary members, to a number not exceeding twenty-five. Such members shall be entitled to attend all meetings and take part in the proceedings, but cannot vote. Honorary members shall be elected in the same way as active members.

ARTICLE VI

Initiation Fee and Annual Dues

Election to membership shall be completed by the payment of an initiation fee of ten dollars.

Each active member shall pay an annual fee, the amount of which shall be decided at each annual meeting.

Honorary members shall be exempt from fees.

ARTICLE VII

Officers

The officers shall consist of a President, Vice-President, Secretary, Recorder [and Editor], Treasurer and a delegate to the Congress of Physicians and Surgeons.

The officers shall be elected annually on nomination by the council.

ARTICLE VIII

Duties of Officers

The duties of the President, Vice-President, Secretary and Treasurer shall be those usual to these officers. The Recorder [and Editor] shall secure the papers read and see that proper notes are taken of the discussion thereon for the use of the committee on publication.

ARTICLE IX

The Council

The council shall consist of seven members, the senior member being chairman. One member of the council shall be elected each year. Four members shall constitute a quorum. The senior member shall retire at the end of each year and shall not be immediately eligible to reelection.

ARTICLE X

Duties of Council

The duties of the council shall be to consider nominations for membership and report them to the Society. The votes of four members of the council shall be required for nomination. The council shall also nominate the officers of the Society and shall decide the time and place of meeting.

ARTICLE XI

Committee of Arrangements

The President, Secretary and the chairman of the council shall constitute a committee of arrangements, the President being chairman of this committee. They shall arrange the details of the meeting and the preparation of the programme, and they shall have the authority to invite guests to attend the meeting and to participate in the discussion.

ARTICLE XII

Publication Committee

The Secretary, Treasurer and Recorder shall constitute a committee on publication, to which shall be referred all papers, reports and other matters intended for publication.

All papers presented shall become the property of the Society.

ARTICLE XIII

Amendment of Constitution and By-Laws

Proposals for amendments of the constitution and by-laws must have been made at the meeting previous to that at which they are voted on, the notice for which shall contain an announcement of the proposed changes. Such changes shall require, for their adoption, an affirmative vote of three-fourths of the active members present.

ARTICLE XIV

Termination of Membership

A member may be expelled from the Society for conduct unbecoming a physician and a gentleman. In such cases, formal charges must be made in writing by two members, which shall be referred to the council.

Membership shall lapse for any one of the following reasons:

(1) Absence from three consecutive meetings without excuse acceptable to the council: (2) failure to present and read a paper for five consecutive years; the Secretary in both these cases shall notify members one year before date of possible lapse: (3) non-payment of dues for two years, two notifications having been sent by the Treasurer.

ARTICLE XV

Quorum

Any number of members present at the appointed time of the annual meeting, shall constitute a quorum for the transaction of ordinary business, but for the election of members, fifteen shall be necessary for a quorum; and for the expulsion of members, or for altering the constitution and by-laws, twenty-five members shall be necessary.

ARTICLE XVI

Order of Business

1. The President shall call the meeting to order and deliver an annual address. In his absence the Vice-President shall preside, and in the absence of all these officers, the chairman of the council.

2. When a general discussion is arranged by the council, the two members appointed to open the discussion shall not occupy more than twenty minutes each; subsequent speakers shall be restricted to ten minutes each.

3. Papers shall not exceed twenty minutes in the reading. In the discussion following the reading of such papers, remarks shall be limited to ten minutes. Should any paper be too long to be read in twenty minutes, the writer must prepare an abstract which can be read within that time.*

4. At the business session the report of the council as a committee on nominations to office and to membership, shall be made, and ballot shall be held thereon.

Adopted May 28, 1909.

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*In order to expedite the publication of the Transactions all members whose papers are to appear in the volume, be required either to have their articles in the hands of the editor before July 1 or to have them in process of publication in some medical journal by that date. In the latter event, the editor of the Transactions is to be notified what journal will publish the paper and reprints or galley proofs are to be furnished to him as soon as possible. (Resolution adopted 1912.)

MINUTES OF THE TWENTY-FOURTH ANNUAL MEETING OF THE AMERICAN PEDIATRIC SOCIETY

Held at Hot Springs, Va., May 29-31, 1912.

The meeting was called to order by the President, Dr. Walter Lester Carr of New York. The following members were present: Drs. Isaac A. Abt, Chicago; George N. Acker, Washington; Samuel S. Adams, Washington; Wm. W. Butterworth, New Orleans; Walter Lester Carr, New York; Howard C. Carpenter, Philadelphia; F. S. Churchill, Chicago; Henry L. Coit, Newark; Percival J. Eaton, Pittsburgh; Rowland G. Freeman, New York; E. E. Graham, Philadelphia; J. P. Crozer Griffith, Philadelphia; S. McC. Hamill, Philadelphia; Alfred Hand, Jr., Philadelphia; Henry Heiman, New York; L. Emmett Holt, New York; John Howland, St. Louis; Charles G. Kerley, New York; J. H. M. Knox, Baltimore; L. E. La Fétra, New York; J. Lovett Morse, Boston; Matthias Nicoll, New York; John Ruhräh, Baltimore; Thos. S. Southworth, New York; Fritz B. Talbot, Boston.

There were introduced as guests, Drs. Henry D. Price, Pittsburgh; Thos. C. McCleave, Berkeley, Cal.; Drs. Henry S. Pole, Edgar A. Pole, Lanier D. Pole, Guy Hinsdale, and Frank Hopkins, all of Hot Springs, Va.; Dr. G. Hudson Makuen, Philadelphia; Dr. McGuire Newton, Richmond, Va.; Dr. H. J. Morgan, and Dr. H. E. Snead, Toledo, Ohio, and Dr. Arthur C. Mason, Newburyport, Mass.

The minutes of the twenty-third annual meeting were adopted as published in the Transactions.

The following papers were read:

1. The President's Address: by Dr. Walter Lester Carr: "The Relation of the American Pediatric Society to the Reduction of Mortality in Infancy and Childhood."

2. Dr. John Ruhräh: "An Epidemic of Sore Throat with Involvement of the Cervical Lymph-Nodes."

The paper was discussed by Drs. Holt, Kerley Hamill, Knox, Talbot, Churchill, Morse, Coit, Eaton, and Ruhräh.

3. Dr. Howard Childs Carpenter and Dr. J. Claxton Gittings: "The Coagulation Time of Blood in Infants and Children."

The paper was discussed by Drs. Hand, Griffith and Carpenter.

4. Dr. Matthias Nicoll: "Inclusion Bodies in the Blood of Scarlet Fever as a Means of Differential Diagnosis."

The paper was discussed by Drs. Kerley, Holt, Butterworth and Nicoll.

5. Dr. J. H. Mason Knox, Jr. and Dr. T. P. Sprunt: "Congenital Obstruction of the Posterior Urethra."

Discussion by Dr. Griffith.

6. Dr. Henry Heiman in collaboration with Drs. Samuel Bookman and Burrill B. Crohn of New York read a paper entitled: "A Study of the Metabolism of Amaurotic Family Idiocy."

7. Dr. J. P. Crozer Griffith: "Infantile Typhoid Fever based on the Analysis of Seventy-Five Cases of Typhoid Fever Occurring in the First Two and a Half Years of Life."

The paper was discussed by Drs. Hand, Morse, Churchill, Kerley, Graham, Talbot, Heiman, Adams, Coit and Griffith.

8. Drs. Fritz B. Talbot and Francis G. Benedict: "Some Fundamental Principles in Studying Infant Metabolism."

The paper was discussed by Drs. Howland, Hamill and Talbot.

9. Drs. Charles Gilmore Kerley and S. P. Beebe: "A Case of Retarded Development Treated with Thymus Extract."

The paper was discussed by Drs. Holt, Ruhräh, Howland, Churchill, Griffith, Heiman and Kerley.

10. Dr. Thomas S. Southworth: "Dextrins and Maltose in Infant Feeding."

11. Dr. John Lovett Morse: "Maltose in Infant Feeding."

The papers of Drs. Southworth and Morse were discussed by Drs. Howland, Abt, Freeman, Holt, La Fétra, Coit, Griffith, Hand, Southworth and Morse.

12. Dr. Henry L. Coit: "A Note on the Effects of Heated and Superheated Milk on the Infant's Nutrition: Recent Investigations."

The paper was discussed by Drs. Hamill, Abt, Nicoll, Eaton, Talbot, Southworth, Freeman, Churchill, Kerley, Griffith, Knox, Heiman, Adams and Coit.

13. Dr. Rowland G. Freeman: "Serum Treatment of Pneumonia in Infancy."

The paper was discussed by Drs. Nicoll, Southworth, Hand and Thomas C. McCleave (Guest).

14. Dr. Frank S. Churchill: "The Wassermann Reaction in Infants and Children."

The paper was discussed by Drs. Nicoll, Holt, Freeman and Churchill.

15. Dr. L. E. La Fétra: "The Employment of Salvarsan in Infants and Young Children."

The paper was discussed by Drs. Holt, Butterworth, Talbot, Abt and La Fétra.

16. Dr. Eaton gave a "Further Report of a Case of Diabetes Mellitus in an Infant" whose history was presented at the last meeting of the Society.

The paper was discussed by Dr. Kerley.

17. Dr. S. S. Adams: "The Influence of Milk Stations on Infant Mortality."

The paper was discussed by Drs. Freeman, Knox, Coit and Adams.

18. Dr. La Fétra presented photographs, *x*-ray prints and the skeleton of "A Case of Fetal Chondrodystrophy."

The following papers were read by title:

1. "The Sources and Paths of Meningeal Infections," by Dr. David Bovaird, Jr.

2. "The Significance of the Pyloric Reflex in the Treatment of True and Pseudopyloric Stenosis," and "A Graphic Chart Method of Studying and Teaching the Principles of Infantile Nutrition," by Dr. David Murray Cowie.

3. "Acute Yellow Atrophy in a Child Three Years Old," by Dr. Francis Huber.

4. "Trials of the Phenolsulphonephthalein Tests for Renal Function in Children," by Dr. Henry D. Chapin.

5. "Concerning Scurvy and Modern Conditions," by Dr. William P. Northrup.

6. "Feeble-Minded Children; What Shall We Do With Them?" by Dr. Charles P. Putnam.

7. "Problems of Infant Feeding Illustrated by Cases and Charts," by Dr. Percival J. Eaton.

8. "Age and Seasonal Incidence of Diseases in Children," by Dr. Charles Herrman.

9. "The Relation of Heat and Humidity to Infant Mortality," by Dr. William Palmer Lucas.

10. "The Code of Standards of the American Association of Medical Milk Commissioners," by Dr. Henry L. Coit.

EXECUTIVE SESSION, MAY 31, 10 A. M.

The report of the council was read by the Chairman, Dr. S. McC. Hamill.

Excuses for absence from the present meeting had been received from Drs. Bovaird, Chapin, Cowie, Dunn, Forchheimer, Gittings, Haynes, Herrman, Jacobi, Jennings, Koplik, Miller, Northrup, Putnam, Rotch and Winters.

The council recommended as officers for the ensuing year for President, Dr. John L. Morse; Vice-President, Dr. John Ruhräh; Secretary, Dr. Samuel S. Adams; Treasurer, Dr. Charles Hunter Dunn; Recorder and Editor, Dr. L. E. La Fétra; Member of Council, Dr. Thomas Morgan Rotch.

As representative of the Society on the committee of arrangements for the next meeting of the Congress of American Physicians and Surgeons, Dr. Samuel S. Adams.

As the place of meeting for 1913, Washington, D. C.; and it was further recommended that the Society convene at 10 a. m., on the day immediately preceding the opening of the Congress.

The council recommended for election to membership in the Society Dr. H. M. McLanahan, Omaha, Neb.; Dr. R. Langley Porter, San Francisco; Dr. Oscar M. Schloss, New York, and Dr. Borden S. Veeder, St. Louis.

It was recommended that the publication committee be authorized to enter into a contract with the American Medical Association for the publication of the Transactions and that this Association be requested to have copies of the transaction on sale.*

It was recommended that a copy of the Constitution and By-Laws of the Society be printed in each volume and that opposite the name of each member there be printed the date of his election to membership in the Society.

It was recommended that in order to expedite the publication of the Transactions, all members whose papers are to appear in the Transactions, be required either to have their articles in the hands of the editor before July 1 or to have them in process of publication in some medical journal by that date. In the latter event, the editor of the Transactions is to be notified what journal will publish the paper and reprints or galley proofs are to be furnished to him as soon as possible.

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* It was found that having on sale copies of the Transactions by the American Medical Association was not practicable.

The council recommended the acceptance of the invitation from the International Congress on Hygiene and Demography to participate in the transactions of the Congress at its meeting in Washington, Sept. 23 to 28, 1912.

It was recommended that the report of the Treasurer, having been audited and found correct, be accepted and that an assessment of $15 be levied as dues for the ensuing year.

It was moved and carried that in the event that required information relating to candidates for membership is not furnished to the Secretary by three months before the time of the meeting at which they would be considered, such candidates for election shall be held over for another year.

It was moved and carried that a committee of three be appointed by the President to confer with the Russell Sage Foundation with regard to its work on infant hygiene and infant mortality.

On motion of the Secretary, a vote of thanks was extended to the President of the Society and to the management of the Homestead Hotel.

Samuel S. Adams, *Secretary.*
L. E. La Fétra, *Recorder.*

THE RELATION OF THE AMERICAN PEDIATRIC SOCIETY TO THE REDUCTION OF MORTALITY IN INFANCY AND CHILDHOOD

WALTER LESTER CARR
NEW YORK CITY

PRESIDENT'S ADDRESS

I appreciate the honor you have conferred on me by electing me to the presidency, as successor to men recognized in the medical profession as leaders in pediatrics.

So many illustrious names are on our rolls that the mention of some of them without giving all would seem an invidious comparison, and it will suffice to state that a list of ex-presidents that contains the names of the late J. Lewis Smith, Joseph O'Dwyer, William S. Christopher and John M. Keating must indicate a society that has set for itself high standards in the forward march of scientific medicine. It is to one part of this advance that I ask your attention briefly so that we may better understand influences that are correlated with the work of this Society and which must inevitably affect its future. I refer to the efforts that are being made to lessen disease and mortality and to improve the physical foundation of infants and children.

The word conservation may be overused, but it has an aptness of expression that brings to our minds the improved conditions that prevail in an awakened public sentiment regarding natural resources and an appreciation of the value of health and life.

In our endeavor to save human life we are in a position where as the foremost society for the study of disease in children in this country we must know pathologic discoveries and also, if we are to be ranked among the pathfinders, have a seeing eye for causative factors of heredity and environment that predispose to the pathologic processes that we are met here to study. These causative factors have never been ignored entirely, but in looking over the Index of the Transactions of this Society it is easy to note the changed point of view of the profession as evidenced by the titles of the papers presented in recent years. Now the topics concern nutrition and problems in metabolism, while formerly the subjects were more often of clinical and pathological interest.

Since its organization in 1888 many influences that have been felt by our Society, and similar medical bodies, have been outside of our direct sphere of activity. Some of these influences have made a change in our attitude regarding disease and we have assimilated them as part of the science of medicine. The lasting fame of Pasteur rests on such influence as to the cause of disease, translated into every-day medical practice. Other influences have exerted pressure on us, but we could not measure their power and, because of the limitation imposed on us by our constitution, we have felt it beyond our sphere to discuss biology, heredity, hygiene and pedagogics.

Pressure, such as I have indicated, has come from discoveries made in all branches of science and also from an understanding of the value of these discoveries by people not in medicine, who in association with medical men have taken up some of the problems regarded formerly as the sphere of the doctor. Physicians have occupied themselves with actual disease and its treatment and have not ventured, except in rare instances, into the larger field of prevention.

Latterly, however, popular knowledge of science and medicine has led to the formation of societies with membership lists of physicians and laymen who have cooperated for the public good along educational lines. One such society, the aim of which has been not only medical but also progressive and educational, has brought to discussion the views of clinicians and sanitarians and by the publicity given to its meetings and publications has aroused popular sentiment and effected many reforms.

In another society physicians have associated themselves with tenement visitors, statisticians, and trained nurses to lessen the death-rate in infancy.

Both of these organizations have had a decided influence in lowering mortality and through their propaganda have acted as conservators of life and health. Boards of health and milk commissions have enlarged the sphere of preventive medicine and their efforts have been reflected in our Society more largely perhaps than in any society of similar character.

Reference is made to these efforts for conservation to show how far the public has advanced in its education and not to revert to the fact that by increasing knowledge that can be understood by intelligent people we give to them the power to combat disease and an understanding of the influence of heredity, environment, infection and lowered resistance.

This broadened information, through the instruction and advice of the medical profession, has curtailed the discussion of etiological factors in this society. It is not that we have destroyed disease nor have we so mastered its symptoms that there are not problems before us to be solved, but what we have done is to spread broadcast a knowledge of the influence of bad milk, of bacteria as a source of intestinal disease, of the disturbances of nutrition as affecting growth and development and of the danger of infection. Making, as we have, in common with other societies, a study of the origin of disease we, as pediatricians dealing directly with the formative period of life, have, without intent on our part, limited our activity along special lines of scientific work because, for a time, we seem to have settled some important problems, so far as concerns their medical side, and we have relegated many topics to semi-medical organizations, over which we exert only indirect control. This is the position we occupy in the broad problem of conservation of infant life.

If we have shifted our responsibility it is still the duty of this Society to keep in touch with all social and economic problems that have to do with the physical foundation of the human offspring. In studying so complex a fabric as the growth of the child, the supervision given by the parents and teachers is not enough to determine its limits of strength and energy. It is not for us to usurp the rights of those who are the natural guardians of childhood, but it is our duty to act as judges and advisors and we can aid in the care of children, who, through no fault of their own, are deprived of the guidance of those who should be their protectors. Infant mortality, child labor, and physical betterment, although interwoven with economic problems, confront us and they become more and more important with a lowered birth-rate, as it is an essential requirement that the surviving members of the race should be endowed with the highest potential efficiency to improve their physical standards and to build on them a more controlled and stable human machine.

Although there are many aspects of these problems that cannot be made part of the regular program of our meetings, we have a responsibility that our organization cannot pass on to those whose knowledge is less definite than ours, nor can we in justice to ourselves and to the community relegate the topics to other societies without giving them our expert advice.

In reply to a circular letter sent by your president to sixty-six members of the society, forty-one members answered. Two of the forty-one indicated that they are not affiliated with any organization or movement for improving the conditions of early life. Of the thirty-nine who are associated with these endeavors many are interested in two or more societies. The answers received show the following: thirty-nine are members of societies for lessening infant mortality; twenty-six are members of milk commissions; fifteen are members of societies for the study and prevention of tuberculosis; six are members of societies for the prevention of venereal diseases: six are physicians to orphan asylums; five are connected with school and college athletic associations; five have to do with schools and school hygiene; four are members of societies for the prevention of cruelty to children; four are connected in some advisory capacity with boards of health; four are interested in playground associations: three are members of kindergarten associations; two are members of societies that have to do with child labor laws; one is a member of a society for the prevention of ophthalmia; one is a member of a children's aid society; one is connected with a children's court; seven are connected with similar organizations that are not classified. Our society through its members is influential, but this is personal and does not represent us officially.

For a better understanding of what is being done to reduce infant mortality, it may be stated that the results of efforts made for child conservation are felt all over the world. In most European countries during the first five years of the twentieth century the nursling mortality was from 5 to 10 per cent. less than in the previous five year period. Allowing as we must, for a falling birth-rate—for example, in Paris from 29 per thousand in 1890 to 24.2 per thousand in 1909—the mortality in infants shows a reduction in the recorded deaths and is evidence of greater care in the handling of the newly-born.

These efforts toward conserving child life are not confined to Great Britain and to Continental Europe, but have extended to the tropics and also to the Canal Zone, where by the care exercised in medical and sanitary matters, there were only eight deaths in 115 cases of enterocolitis admitted to the hospital between January 1, 1906, and March 1, 1911.

Through the assistance of Dr. W. H. Guilfoy, registrar of the Department of Health of the City of New York, I am able to give the mortality record of the city as follows:

Deaths and rates per 1,000 children living under one year of age, comprising the years since the formation of the greater City of New York.

YEAR	DEATHS	RATE
1898	16,070	203
1899	15,381	182
1900	16,640	192
1901	15,467	173
1902	15,526	168
1903	14,413	151
1904	16,125	164
1905	16,522	163
1906	17,188	164
1907	17,437	160
1908	16,231	144
1909	15,976	137
1910	16,212	134
1911	15,030	120

If we compare the rate of 1898 with that of 1911, we will obtain a decrease of slightly over 40 per cent. If we compare the rate of 351 per 1,000 for the months of July, August and September of the year 1898 with the rate of 145 per 1,000 of the corresponding months of the year 1911, we find a decrease of almost 60 per cent.

In order to eliminate the effect of an unfair comparison of a light year with a heavy year as to mortality, let us combine the five years 1890 to 1894 inclusive and compare the average mortality from certain causes of those years with that of the average mortality of the five years 1907 to 1911 inclusive, with the following results:

Taking first the group of contagious diseases, measles, scarlet fever, whooping-cough and diphtheria, the average mortality per 1,000 in the quinquennium first mentioned was 13.19 against 6.10 in the last quinquennium, a decrease of 54 per cent.

The tuberculous diseases, exclusive of pulmonary tuberculosis, average 7.57 per 1,000 in the first quinquennium against 2.19 in the last quinquennium, a decrease of 71 per cent.

Simple meningitis showed a decrease of 76 per cent.; convulsions a decrease of 68 per cent.

The three great groups of diseases affecting infant mortality are the acute respiratory, the diarrheal and the congenital. A comparison of the acute respiratory, that is, acute bronchitis, broncho-pneumonia and lobar pneumonia, shows a drop from 42.83 per 1,000 infants to 29.02, a decrease of 32 per cent. All diarrheal diseases combined show a decrease from 67.58 to 38.37, a decrease of 43 per cent. The congenital diseases, including malformations, premature births, preternatural births, inanition, marasmus and congenital debility, showed a decrease from 60.97 per 1,000 to 51.74, a reduction of 15 per cent.

The mortality from all causes decreased from 229.46 to 146.25 per 1,000 infants, a decrease of 36 per cent.

The only cause which showed an increase was that of syphilis, which increased from 1.73 to 2.25 per 1,000 infants, an increase of 30 per cent.

One group of disease, the diarrheal, showed a higher decrease per cent. in the mortality than either of the other two prominent groups, and would warrant the conclusion that the work of the Department of Health in the supervision of the milk supply and the establishment of milk booths has contributed largely to this result. We must take into consideration all the other factors that have had a bearing on the reduction of infant mortality, the work of the philanthropic societies of the city, the education of the mothers as to the feeding of infants, establishment of parks, etc.

We take into consideration also that the mortality percentage of different years is subject to an up-and-down curve that is incident to all statistics bearing on the death-rate, and that the year 1911 was remarkable as a "light year," during the summer months. With due allowance for this variation in the death-rate, we may, I believe, see some results of the discussions of our society in the improvement in mortality quoted above. We cannot claim all that is good in the lowered mortality rate recorded, because many causes of a lowered mortality were not discussed by us, but other topics incident to it were worked out in our meetings after prolonged deliberations. We took laboratory reports of bacteriologists and of physiologic experimentors, and checked them off with clinical observations, and our conclusions were given to the medical profession, and through them to the general public. By a constant repetition as we elaborated for our own benefit some of these problems, we impressed physicians and laity with the fact that prevention of disease is possible, and a study of cause is better than treatment of effect. Although we had held nominally to this belief, it was not reiterated emphatically as coming

from pediatric authority, and it seemed to require a worldwide movement outside of the medical profession and societies like our own to bring about an effort to save infant life and to develop the best results from our knowledge.

Three things, I believe, are essential to the future of this society to insure its vitality and usefulness:

First, to add to our study of diseases observed in infancy and childhood from the standpoint of their pathological and clinical histories, comparative and tabulated records and methods of precision, so we may judge more accurately of the semeiology of disease. Our collective investigations on scurvy and epidemic poliomyelitis could be extended to other topics, bearing always in mind that every scientific topic is subject to review, and there is none immutable and fixed.

Second, a program on matters relating to metabolic processes, more especially to those of infancy and early childhood, arranged so that investigators will present to this society for its discussion the results of laboratory investigations that bear on our clinical studies.

To this suggestion for the future activities of this medical body, it seems to me we should give much thought. Metabolism comprises so many processes in the development of the body and it points to so many fundamental physiologic facts that we are at times overwhelmed. From the nature of investigations made necessary along the lines of development and physiologic growth, the laboratory offers the best field for experimental study and the pure clinician should await the deductions of the members of this society who are laboratory investigators. Some of the results, however, are valuable clinically and agree with observations that have been recorded by physicians outside the laboratory. Salle, in laboratory experiments, has shown the influence of heat on young dogs and the results of his experiments have accorded with the tables made by Seibert and others, giving the incidence of digestive disturbance in infants during the heat of summer. Many experiments on metabolism are as yet of limited value because they are links of an incomplete chain, the strength of which we cannot judge until it is fully forged, but as West said in 1847, "the child's body is daily undergoing modifications to fit it for new duties as well as daily growing in size and strength," and we want the aid of deductions from laboratory investigations to enlighten us in preparing the child for its future.

Third, an endorsement of movements having to do with physiologic and economic problems relating to infancy and childhood, particularly

those of mortality and disease, in which efforts so many of our members are personally interested. Congenital diseases are among those that may be brought under this class. Dr. Josephine Baker, of the Department of Health, New York City, states a way must be found to diminish the mortality from congenital debility. In this and along other paths that lead to a greater strength for the child and the race, I feel sure that we can work without changing the character of our organization or lessening the value of its meetings.

This society is recognized among the individual members of the societies whose purpose has been indicated above. We can widen our sphere of influence by having representatives appointed to affiliate with organizations having to do with the physical betterment of the child. Advised by the council, such representatives from this society would confer on problems of social, economic and pedagogic importance and would be ready to present information of the physical needs of the growing child and the dangers of pathologic influences.

The American Pediatric Society cannot stand as the highest pediatric body in this country if it fails to recognize the many influences that are laboring both on this continent and in Europe to lower the mortality of infancy and childhood; nor can its opinions be made authoritative unless it acts officially to cooperate with other agencies that are attempting to bring mortality and morbidity under control.

"Pediatrics is preventive medicine of the highest order, and is only possible because of the existence of the developmental period of human life, and because this development can be acted on, and acted on strongly by environment, either advantageously or disadvantageously."[1]

If we believe this we cannot, as a scientific body, neglect our opportunities, and we should be ready to give hearty aid and approval to those societies that approach pediatrics from standpoints other than medical.

68 West Fifty-First Street.

1. Christopher: "The Keynote of Pediatrics." Presidential Address Before the American Pediatric Society, [1902]

A BRIEF REPORT OF AN EPIDEMIC OF SORE THROAT WITH INVOLVEMENT OF THE CERVICAL LYMPH-NODES

JOHN RUHRÄH, M.D.
BALTIMORE

There have been reported from time to time in European cities certain epidemics more or less associated with the milk-supply. Some of these epidemics have had a clinical picture which is more or less characteristic and which has been called by the English observers septic sore throat. The report of the United States Public Health Service records eight epidemics that occurred in England, the first in 1881 and the last in 1905. Bacteriologic examinations were not made in all these, but in the cases so studied the streptococcus was found. In seven of the eight epidemics one, or more, cows was discovered suffering from mastitis or from an eruption of the udder. In 1908 there was a remarkable epidemic which occurred at Christiania; this was found to be due to one milk-supply, and one cow was discovered with a diseased udder. From the cow there was isolated a streptococcus which was found in every way identical with the streptococci obtained from the patients suffering with the disease. The methods in use at that time for differentiating the varieties of streptococci were not as good as at present and even our present methods leave much to be desired.

Similar epidemics have been reported in other foreign cities. The first outbreak of this kind in the United States with which I am familiar occurred in Boston in 1911. This epidemic was one of unusual severity, affected chiefly adults, and was finally traced to one of the largest and best controlled dairies supplying milk in Boston. This year, in the month of February, a similar infection was noted and Dr. Mark Richardson, secretary of the Massachusetts State Board of Health, in a letter writes: "We found at a milk depot of this firm conditions which we thought explained it. At any rate we requested that all the milk from this special milk depot be pasteurized, and the epidemic promptly ceased."

A similar outbreak occurred at Concord, N. H., and Davis and Rosenow reported a large number of cases that occurred in Chicago.

In Baltimore the epidemic began early in January. Curiously enough, one or two cases presenting exactly the same clinical picture were observed in December. The cases increased throughout February and in the third and fourth weeks became very numerous. After the first three weeks of March were over very few of the typical cases were noted, although there was a large number of cases of sore throat from which streptococci could easily be isolated, but which were free from the complications that characterized the epidemic.

Dr. Louis Hamburger was one of the first to recognize the epidemic as milk-borne, and the subject of the disease was talked over at a meeting called at his suggestion. The results of his experiences were charted and they showed conclusively that a great number of people were using milk from one of the largest dairies in the city. For example, in two homes for trained nurses one used milk from the suspected dairy and showed a percentage of 71.4 of the inmates suffering during the epidemic from some form of sore throat; this is in striking contrast with 8.3 per cent. in the other home which was using milk from another dairy. In sixteen fatal cases it was found that fourteen used milk from the suspected dairy, and that in two the milk-supply was unknown. Both of these unknown cases occurred in adults, one before the milk-supply was suspected, and the other was in a hospital patient who was too ill to be interrogated.

Another method of studying the relation of the disease to the milk-supply was by taking a group of households using the infected milk and a similar group, taken at random, using other milk, the only requirement in the cases so taken being that the households should contain two or more children. The results were about the same as that shown in the nurses' homes.

Subsequently the disease was studied by Dr. Frost of the United States Public Health Service, and the results of his investigations will be published in a separate paper. He found, however, that in about 80 per cent. of the cases which occurred from the middle of February to the middle of March the patients were using milk from a suspected dairy. He was able to find some 600 undoubted cases of the disease, but this represented only about one-third or one-fourth, or even a smaller percentage, of the actual number of cases which occurred during the epidemic. In these 600 odd cases there were twenty-eight fatalities and twenty-two of these had used milk from the suspected dairy.

An interesting point in relation to the suspected dairy in the Baltimore epidemic was that previous to the epidemic the flash method of

pasteurization had been used. Wishing to make some repairs and improvements in the pasteurizing room, pasteurization was stopped during a considerable portion of the time in January and February and in the first part of March. The weather during this time was extremely cold and it was thought that the repairs and improvements could be made more safely at this time than at any other season of the year. Following the announcement that the epidemic was caused by milk a holding pasteurizer was installed and after this the epidemic promptly ceased. About this time, however, it should be borne in mind that the public was repeatedly warned through the daily papers to boil the milk, and a very large number of people using milk followed this direction and this undoubtedly had much to do with the prompt cessation of the epidemic.

The Baltimore epidemic differed somewhat from the others which have been described, in that children were very largely affected, fully 50 per cent. of the cases occurring in early childhood. Cases were noted in children as young as 4 months, and Dr. Hamburger had one case at 65 years of age, and he also stated that he knew of one case, which was not included in his series of cases, in which the patient was 86 years of age. In my own cases, all in children, almost all of them occurred between the ages of 12 and 24 months.

There seems to be little doubt that the disease was originally derived from using contaminated milk, but once having been started it was possible to have the disease transmitted in the ordinary ways. It frequently happened that all the members of a household would be affected, but for the most part the adults escaped with light attacks. In a number of instances nurses in constant attendance on the children became affected and had typical attacks. In one instance a cat which drank freely from the infected milk was affected very much in the same way that children were, that is, with an angina and enlargement of the cervical lymph-nodes.

Bacteriology.—I am indebted to Dr. Standish McCleary for the following information: The organism, frequently in pure cultures, which was seen in smears made from these patients, was a diplococcus with a distinct capsule, easily demonstrable with the usual capsular strains. The diplococcus was Gram-positive. When grown on all mediums this capsule disappears but returns after passage through mice. When cultivated the organism takes the form of a streptococcus in short chains in which the diplococcus arrangement is preserved. Occasionally tetrads are seen. On slant agar a thin, slightly moist dewlike colony is obtained. Hemolysis

occurs on blood-agar. Litmus milk is acidulated and coagulated and broth is rendered turbid. Lactose and saccharose are fermented but not inulin. The thermal death point in milk is 54 C. at an exposure of twenty minutes. The organism is found in the pus of the otitis which occurred so frequently, and also in the suppurating lymph-nodes, which were not frequent. In some cases the pneumococcus was obtained from the throat, sometimes in pure culture.

The Clinical History.—There are four classes of cases met with — mild cases, cases of average severity, severe cases, and cases of unusual intensity, usually owing to some severe complication occurring at the onset.

The mild cases were for the most part in adults and many were not sufficiently ill to go to bed; very few of these came under my personal observation. They were characterized by an angina of mild intensity, and for a day or two slight enlargement of the cervical lymph-nodes. There was slight fever, headache and general malaise. These symptoms persisted for several days and then usually from two to three weeks would elapse before the patient felt quite well, and many complained of slight recurrence of the symptoms, lasting twenty-four hours or more. There were some mild cases in children; by far the greatest number, however, presented the same clinical picture. There was sudden onset with fever, and occasionally a convulsion; the temperature varied from 101 to 104 or 105 F., and there was considerable prostration. At the outset the only physical sign of any importance was the general redness of the pharynx and pillars of the fauces; this was usually a dusky red and at some places there were slight patches of exudation, particularly on the tonsils. This exudation could easily be mistaken for diphtheria but was not nearly so adherent, and much of it consisted of pus which could easily be wiped off. In other cases there was the typical appearance of a tonsillitis, the crypts being filled with a more or less hard and purulent material. Children old enough complained of pain usually located in the head, neck or abdomen. After two or three days there was marked swelling of the lymph-nodes at the angle of the jaw. These were almost always on both sides and varied in size from a hazel nut to a pigeon's egg, or even larger. There was more or less exudate into the subcutaneous tissues, and these swellings were painful and tender to the touch; they persisted for two or three weeks and gradually subsided, in most instances leaving the nodes normal in size or very slightly enlarged. The fever and prostration varied greatly, the mild cases lasting a week to

ten days; some of the more severe cases continued as long as two weeks, and sometimes longer.

The severe cases came on with great intensity, usually either with a chill, or more commonly with a convulsion, the temperature rising rapidly to 106 or 107 F., and sometimes even higher. The appearance of these children was very alarming, the pulse was rapid and weak and the respirations irregular and shallow. There were marked pallor and more or less cyanosis; in some there were marked vomiting and sometimes diarrhea. After a day or two the lymph-nodes at the angle of the jaw enlarged and usually this was coexistent with an improvement in the general condition. In many of the severe cases there were complications as noted below.

The worst class of cases either started with very severe symptoms or sometimes these symptoms came on two or three days later. In these cases there was no enlargement of the lymph-nodes, or the enlargement was slight, and the general clinical picture was that of a septicemia with very high, irregular temperature, great prostration, usually numerous complications and death. Certain other cases were characterized by the appearance of a peritonitis which was apparently only a complication in the course of the septicemia. The fatal cases are striking, the usual history being of a child in perfect health taken with a convulsion and high fever and slight redness of the throat; the child was either comatose or partially so; there were generally vomiting and diarrhea and distention of the abdomen, which later became very tender, and then a considerable rigidity of the muscles developed; within forty-eight or seventy-two hours after the onset the child would die, sometimes from failure of respiration, occasionally from failure of the heart.

Complications.—The complications attending this disease were remarkable for their number and their intensity; most common of all was the inflammation of the middle ear, which occurred in from 30 to 40 per cent. of the cases. Next to this were irregular swellings, sometimes suggesting an edema, at other times suggesting abscess formation, although these swellings rarely suppurated. The swellings were most frequently noted about the throat over the epiglottis, or at the base of the tongue at the side, sometimes in the floor of the mouth, sometimes posteriorly in the pharynx, suggesting retropharyngeal abscess. Suppuration was not a very common thing in my experience, apart from the inflammation of the middle ear, and in only two instances did the lymph-nodes in the neck suppurate, and in one of these the suppuration evidently

followed a retrotonsillar abscess. In one instance there was a retropharyngeal abscess, and in one other case numerous points of suppuration occurred apparently independent of the swollen nodes. Edema of the eyes, affecting both lids and the tissues about the orbit, was not uncommon, and this usually, although not always, was unilateral and accompanied with nothing more than a slight conjunctivitis with little or no discharge. Bronchitis was not uncommon, and quite a number of patients had pneumonia as a complication. Gastro-intestinal disturbances were also common, usually consisting of vomiting and a very irritable stomach, and later on a more or less intense diarrhea. In three cases there was an erysipelas, two occurring on the scalp and one on the face. These ran a typical erysipelas course and finally stopped suddenly. In some cases the joints were swollen, and in some others the tissues about the joints, the joints themselves remaining more or less free. In some cases there were petechiæ, and in others larger ecchymotic spots, and in one instance there occurred about the tenth day very large subcutaneous hemorrhages, as if there had been an actual rupture of some of the larger vessels and which suggested the rupture of the vessels which has been noted in experimental work in pneumococcus infections. In one instance the hemorrhages occupied both sides of the scalp, and also the arm from the wrist nearly to the shoulder, the swelling thus produced being larger than one would imagine was possible.

CONCLUSIONS

The lessons to be learned from this epidemic are as follows:

1. A streptococcus infection may be caused by infected milk, and this disease may be exceedingly severe and attended with numerous complications and fatalities.

2. Even in cold weather milk may be the source of the disease.

3. No matter how carefully raw milk is handled it may at times be a source of danger.

4. The milk supplied to cities should be pasteurized, and where by accident the dairy company cannot properly pasteurize its milk, it should be compelled to notify its consumers, so that they can either pasteurize or boil the milk.

DISCUSSION

DR. HOLT asked whether it was discovered how the disease got into the milk and what was the condition of the employees.

DR. KERLEY said that Dr. Ruhräh's remarks interested him very much. In the capacity of consultant he saw a case in Brooklyn, recently, that was some-

what similar to those mentioned. The first sign of illness was a sore throat with moderate redness but no exudation on the tonsils or elsewhere. This was quickly followed by a very considerable swelling of the glands on both sides of the child's neck. This in turn was followed by a mild pneumonia from which the child made a good recovery. The glands also subsided, from which the child made a good recovery. The patient then developed on about the sixth or seventh day of the illness, a peritonitis of a fairly severe type. Greatly to the surprise of the attending physicians, the peritonitis apparently subsided and the abdomen became soft and relaxed. The child now developed an acute nephritis with casts, blood and albumin in the urine with a complete suppression that lasted for twenty-four hours. This condition improved and again the child seemed to be doing well. Three weeks had already been covered in the illness. After the kidney resolution the peritonitis returned, from which the child died after four weeks of illness. The case corresponds very closely with those described by the reader of the paper.

DR. HAMILL understood that the final decrease in the number of cases was attributed to the repasteurization of the milk from the dairy which was thought responsible for the epidemic, but he wished to know what the decided fall during the first week of March, as indicated in one of the charts, was due to. He asked if this dairy gathered milk from a large number of farms, and whether they traced the source of the epidemic to some one cow or group of cattle.

He considered the market creams in general more dangerous than the market milks, as they were apt to be older and less carefully handled. He called the attention of the Society to the fact that at the last meeting of the American Association of Medical Milk Commissions, a standard for the certification of cream, corresponding in all details except in its fat content to the requirements for certified milk, had been adopted.

DR. KNOX said that he had been interested in the epidemic described by Dr. Ruhräh. There were only one or two points that he wished to emphasize. One was the complication of erysipelas. He had seen two fatal cases. In both there was only a slight reddening of the throat and no enlarged cervical glands. In each case the temperature was markedly and continuously elevated—104 to 106 F. In a third instance, in a marantic infant, the temperature remained lower, varying from 101 to 103 F. In this latter case, the condition was not at first recognized. When the child was first seen it had on each shoulder a raised, slightly reddened area 3 or 4 cm. in diameter, without any surrounding blush. After twenty-four hours, the nature of the affection became known, as from the original areas on the shoulder, there was a rapid infiltration of the skin, extending down both arms and reaching the fingers. The child was extremely ill for four or five days, but afterwards made an uninterrupted recovery. The other point he referred to was the possible relationship of this infection to clinical scarlet fever. A case was reported of a boy 5 years old. He was very ill. Typical symptoms—sore throat, high fever, enlarged cervical buboes, more marked on the right side. Subsequently a double otitis media developed. His fever persisted for two or three weeks. There was some abdominal tenderness, and fear was entertained of possible peritonitis. The spleen was extremely large, larger than Dr. Knox had ever seen except in cases of splenomegaly or malaria. When the fever subsided the size of the spleen rapidly decreased. The child finally made an uninterrupted recovery, and went to Atlantic City, presumably well. After a few days, the purulent discharge from one ear returned. The ear was irrigated by the child's mother three times a day. She developed an infection of the middle finger of the left hand.

The pus from this infected area contained the same organisms as were found in the child's ear. Shortly after this, the mother's throat became sore, and from the tonsils the same organism was obtained. Four days after the throat infection the mother developed typical clinical scarlet fever. The rash covered her whole body and persisted for a week. Her temperature remained between 102 and 104 F. for five days, and after ten days quite an extensive desquamation occurred. One or two other physicians agreed in the diagnosis of scarlet fever. Without a doubt the infection of both mother and child was due to the same organism, which was an atypical streptococcus, such as Dr. Ruhräh has described.

DR. TALBOT, reported that during the summer of 1911 there were many more cases of streptococcus diarrhea on the Boston Floating Hospital than ever before. The diagnosis was made by the bacteriologist. In a large proportion of these cases pure cultures of streptococci were found in the urine.

DR. CHURCHILL said that they were having a similar epidemic in Chicago, which was being carefully studied. He was chiefly interested in cases that occurred in his own children who proceeded to hand the disease on to him. These patients had certified milk and cream. Most of the cases in Chicago were traced to a particular milk. Just how far they had gotten in their study he did not know, but the epidemic could not be attributed entirely to one particular delivery. The infection was severe and it attacked many physicians. In his own case the disease began in the glands of the neck. In all the cases streptococci were found.

DR. MORSE said that two similar epidemics had occurred in Boston, one in the spring of 1911 and one this last winter. The one occurring in 1911 was a severe one and gave everyone a new conception of the seriousness of tonsillitis and sore throat. The epidemic was not only traced to a single milk supply, but to one man who handled the milk. The man himself had a sore throat. The epidemic that occurred last winter was presumably connected with the same dairy, but it had not been proven. The striking thing in the Boston case was not the severity of the original infection, but that of the complications, such as endocarditis and general peritonitis, undoubtedly due to the blood-infection. The cases with peritonitis were almost invariably fatal, whether operated on or not. In the epidemic of this year there had been a large proportion of glandular enlargements; only a very small proportion of them suppurated, but when suppuration did occur it was not superficial but deep, and one gland after another often became involved

DR. EATON asked regarding the treatment employed and whether autogenous vaccines had been used.

DR. RUHRÄH closed the discussion. In answer to Dr. Holt he said that a certain amount of investigation had been made but they could not determine how the disease got into the milk. Some of the Health Department inspectors were working on this problem but so far they had nothing to offer. In England it was found that the disease originated from abscesses or other diseased conditions about the mammary gland. In Christiania an epidemic was traced to one cow in a herd; they found a streptococcus that was identical with the streptococcus that caused the sore throat. With regard to the Baltimore epidemic he could not say how the disease got into the milk; it was plain that it was the milk that was causing the trouble. In answer to Dr. Hamill, he replied that the fall was more apparent than real; he thought the fall occurred in the children who already had the disease. In his experience the more severe cases appeared about February 14, and up to March 17 there were many cases. In regard to Dr. Knox's discussion, he said that in this epidemic a few of the children had a rash that was strongly suggestive but not at all typical of scarlet fever. It faded away more quickly.

With regard to the question of the nature of the organism, he stated that this could not be definitely answered at this time. In nearly all the cases studied the streptococcus could be easily isolated and in some a pneumococcus was found. There was considerable discussion in Baltimore concerning the relation of the pneumococcus to the disease. In many cases, however, the streptococcus seemed to be the sole cause of the trouble. The death point of this organism in the milk was a temperature of 54 C. employed for twenty minutes. In answer to Dr. Eaton he said that the therapeutic measures employed were of a general nature, and apart from these, unsatisfactory. No vaccines had been used so far as he knew. Hydrotherapy was used in the cases with a high temperature sometimes without affecting the unusually high temperatures, some of which reached 106 and even 108 F. Hexamethylenamin was used in some cases but had little or no effect.

THE COAGULATION TIME OF BLOOD IN INFANTS AND CHILDREN

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The value of a reliable yet practicable method for the determination of the coagulation time of blood is obvious, yet the amount of experimental work expended on it within recent years testifies to the difficulties inherent to most of the clinical methods which have been devised.

The large majority of observations, however, have been made on adults, so that it seems desirable to extend the study to infants and children, both in health and disease, in order to decide, if possible, on a standard for comparison.

Before presenting the conclusions of other authors and the results of our own work, we may consider briefly the various coagulometers in use, with an equally brief discussion of the most important and established factors of error more or less inherent to any clinical method.

A recent article by Myer Solis-Cohen contains such a thorough consideration of instruments and methods that it would appear to be a work of supererogation to present another résumé. We may take this opportunity of acknowledging our indebtedness to him, both for the collaboration of the results, and for his extensive and complete bibliography which brings the literature of clinical methods up to a recent date.

According to Solis-Cohen, these methods may be divided into classes, according to the principles employed. We have rearranged his classification as follows:

1. Methods in which the blood is drawn into capillary tubes.

2. Methods in which the corpuscles are set in motion by a current of air or oil directed against the drop.

3. Methods in which the blood is collected on one or more wire loops.

4. Coagulation time determined by formation of film.

5. Coagulation time determined by observing changes in contour of drop.

6. More or less complex methods, necessitating the employment of activated serum, anticoagulant substances, etc.

With such a diversity in technic, it is plain that each individual method in the various classes must be interpreted in terms of its own normal time limit for coagulation, to which must be added the variation dependent on the personal equation of the investigator who employs it.

For example, the accompanying table (Table 1) compiled by Solis-Cohen, emphasizes the truth of this statement.

TABLE 1.—NORMAL CLOTTING-TIMES OBTAINED WITH DIFFERENT METHODS

Method Employed	Clotting-Time Obtained, Minutes
Class I—	
Vierordt's	9½
Wright's	2½ to 5
McGowan's	8
Addis' modification of McGowan's	9½
Rudolf's modification of McGowan's	8½
Sabrazés'	9 to 10
Schultz's	5
Class II—	
Brodie-Russell	3 to 8
Pratt-Grützner modification of Brodie-Russell	3 to 8
Bogg's modification of Brodie-Russell	3 to 8
Addis' modification of Brodie-Russell	8
Class III—	
Biffi's	7 to 10
Goldhorn's modification of Biffi's, about twice as long as above	
Buckmaster's	5¾
Class IV—	
Slide and Straw	2½ to 5
Schwab's	4¾ to 5½
Bürker's	6 to 7
Riebe's modification of Bürker's	12 to 14
Class V—	
Hayem's	3 to 20
Milian's	15 to 34
Bezançon and Labbé's modification of Milian's	10
Hinman and Sladen's modification of Milian's	5 to 8
Duke's modification of Milian's	5 to 7
Solis-Cohen's modification of Milian's	8⅔
Class VI—	
Morawitz's	5

It is evident that many factors are concerned in the production of such wide variance in results. The most important of these may be considered briefly.

CONTACT WITH A FOREIGN BODY

It has long been recognized that coagulation of blood is hastened by contact with any foreign body other than a pure oil or paraffin. With proper precautions to exclude these foreign factors, including air, the

coagulation time can be immensely lengthened. In the use of clinical methods it is clearly impossible to exclude them. In the hands of a practiced operator, however, these errors should be approximately the same for each method. The variable factors over which we can exert no control are the atmospheric conditions and the viscosity of the blood. The other factors, which may be variable in the case of the novice, but which are obviated largely by the skill resulting from constant practice, are, (1) presence of dirt on the site of puncture or on the instrument; (2) pressure on the tissues surrounding the puncture; (3) depth and width of the puncture with their influence on rapidity and volume of the flow; (4) amount of blood withdrawn; (5) length of time in which the blood remains in contact with the tissues; (6) the temperature at which the blood is allowed to coagulate; (7) the shape, diameter and depth of the drop under observation; (8) end point adopted.

The last three factors vary according to the method employed, as well as with the skill of the operator. It is altogether probable that other factors exist of which we have no accurate knowledge. The foregoing list contains the chief sources of error which affect the clinical methods now in use.

Granting that the site of puncture and the instrument shall be absolutely clean, that the puncture shall be deep and wide enough to permit of free and rapid flow and that no pressure shall be made on surrounding tissues, we may consider the remaining factors.

The influence exerted by the amount of blood withdrawn is obviously connected with the well known fact that the coagulation time lessens, the longer the flow of blood. Of equal and similar importance is the influence of contact with the tissues—the longer the contact the shorter the time required for coagulation.

The remaining factors are inherent to individual methods. The concensus of opinion indicates that the effect of temperature is of extreme importance, heat hastening and cold retarding coagulation time. The necessity of making provision for the maintenance of body temperature during the time the blood is under observation seems to us so obvious that we have employed none of the simple but inaccurate methods by which the blood is exposed to the varying temperatures of the room.

The importance of the size and depth of the drop has been emphasized, but, we think, insufficiently. A further consideration of this may be postponed.

That the end-point adopted for the different methods by various operators must affect the published reports likewise is obvious. In general, it may be said that the method which permits of the easiest and least disputable interpretation, possesses the greatest practical advantage.

It would be of advantage to consider at greater length those factors which exert the greatest influence on the coagulation time of blood with whatever method observed, namely, the amount of blood withdrawn and the duration of its contact with the tissues. These depend on the intrinsic phenomena of coagulation *per se,* and, therefore, are inseparably connected with the method of securing blood by puncture of the skin.

From the chaos of ideas produced by the vast amount of experimental work on the problem of the coagulation of blood, a fairly clean cut theory has been evolved, due principally to the studies of Morawitz and Fuld, and Mellanby. It may be stated as follows:

The factors essential to coagulation are the following:

1. Fibrinogen, one of the component parts of blood, belonging to the group of globulins.

2. Prothrombin, also present in the blood, but of unknown chemical composition. It exists in a condition of absorption in the fibrinogen molecule (Addis).

3. Ionizable calcium salts, present in the blood.

4. Antithrombin, a hypothetical substance which exists in the circulating blood. It is probable that its counterpart exists in the antithrombin which has been isolated in approximately pure form from the salivary glands of the leech. This is a soluble protein resembling the peptones and proteoses (Howell). Certain it is that a substance with antithrombic characteristics is found in "peptonized blood."

5. Finally, there is a substance known as thrombokinase (thromboplastin), of unknown chemical composition, which is present in all the body tissues, especially those rich in nucleoprotein, and in the formed elements of the blood (platelets), but is not found free in the circulating blood.

The first four substances are supposed to be present in normal circulating blood at all times. The last, kinase, appears when there is injury to body tissues or to formed elements of the blood.

According to the theory we are discussing, when prothrombin and thrombokinase come into contact in the presence of ionizable calcium salts, there is formed, after a short interval, a substance known as

thrombin, which unites instantly with fibrinogen to form fibrin — the substructure of the blood-clot. From its power to prevent the formation of this substance, thrombin, the so-called antithrombin gets its name.

According to Addis, on account of the close molecular relation which exists between this newly-formed thrombin and fibrinogen, the thrombin escapes the neutralizing action of antithrombin, and fibrin is quickly formed from its action on the fibrinogen. "Most of the thrombin is precipitated with the fibrin. . . . That part of the thrombin which is not so precipitated is gradually neutralized by the antithrombin." As Mellanby points out, "The whole mechanism of coagulation is admirably adapted to produce large and rapid clotting within a wounded area, but to stop the process immediately beyond the confines of the injured tissues" (by means of the antithrombin).

Since injury to the tissues by puncture at once makes the thrombokinase available, it is easy to see the importance of the above-mentioned factors of error in clinical determinations. The longer the blood flows and the longer the individual drop remains in contact with the tissues, the greater the amount of kinase and the more copious and rapid the production of thrombin, with the consequent shortening of the coagulation time.

On the basis of this simplified theory, Addis constructs a most plausible hypothetical explanation for the hitherto baffling phenomena of the slow or imperfect coagulation seen in the subjects of hemophilia.

Quite recently the work of Howell has cast justifiable doubt on the acceptance of the conclusions of Morawitz and Mellanby.

Howell's theory rests on two facts. "First, the presence in the circulating blood of a constant amount of antithrombin; secondly, the proof that this antithrombin is antagonized or neutralized by the thromboplastic substance (thrombokinase) which is found in tissue extracts."

According to Howell,

> We may believe that circulating blood contains normally all the necessary factors for coagulation, namely, the fibrinogen, the prothrombin, and the calcium, but these factors are prevented from reacting, that is to say, the calcium is prevented from activating the prothrombin by the presence of antithrombin, which is also a constituent of the circulating blood. When blood is shed this antithrombin is neutralized by the thromboplastic substance (thrombokinase) furnished by the wounded tissues and the disintegrating platelets.

In this theory we find an altered conception of the functions of thrombokinase and increased importance is given to the amount and activity of antithrombin. The sole function of the kinase lies in its power to

neutralize antithrombin and thus permit calcium and prothrombin to form thrombin. The conception of the action of thrombin on the fibrinogen to form fibrin, remains unchanged. The source of thrombokinase in tissues and blood likewise remains undisputed.

A discussion of the merits of these two theories would serve no useful purpose. They are presented in order to convey the more recent views on this important and complex problem of blood coagulation. There are methods at present available for isolating four of these substances, fibrinogen, thrombin, antithrombin and thrombokinase. The study of the individual case of deficient coagulation according to more advanced standards must be pursued along these lines. Deficiency of one or more of these substances can be inferred, if not always definitely proved, by such studies as those of Whipple, and Schloss and Commiskey in cases of hemorrhagic disease in the new-born. Nevertheless, it seems important to decide how far the clinical method in the hands of the practitioner unskilled in advanced technic, can be trusted to establish the presence or absence of a delayed coagulation time, and to compare results in the young with those in the full-grown.

Whether we accept the action of the thrombokinase of the injured tissues, as an activator of prothombin and calcium, or as a neutralizing agent for antithrombin, does not affect the clinical method *per se,* since, in either case, excess of the kinase in the shed blood due to faulty technic in collecting the sample of blood will shorten the coagulation time.

CLINICAL METHODS

We must consider next the clinical methods which we have employed in the examination of our cases and the reasons for their selection.

Excluding all those methods which fail to make provision for maintaining bodily temperature, the essential qualifications seemed to be: (1) ease and rapidity of technic; (2) ease of determining the end-point; (3) uniformity in the size and depth of the drop.

For ease and rapidity of technic two types of methods present manifest advantages—those in which the drops of blood are collected on a smooth flat surface of glass, and those in which they are collected on platinum wire loops.

Of the methods in which the blood is collected on glass, that of Brodie-Russell and of some modification of Milian's use of the glass slide seem to have the most adherents. The principle of the Brodie-Russell method depends on the visible motion of the blood corpuscles, impelled by

a current of air from compression of a rubber bulb. This technic introduces manifest and variable sources of error.

Probably the most reliable clinical method which has been devised is that of Addis, in which he substitutes for intermittent jets of air at variable temperature, a continuous stream of filtered mineral oil at constant temperature. The apparatus for this method presents the disadvantage of expense, while facility in operating it requires practiced skill somewhat above the average.

We have confined ourselves to the use of the Solis-Cohen modification of Milian's method and to the wire-loop method of Biffi. The latter permits of obtaining greater uniformity in the size and depth of the drops, while the former may possess some advantages over the loop method in determining the end-point.

In Solis-Cohen's method, four drops of blood, from 5 to 7 mm. in diameter, are collected on the lid of a Stender-dish, and the dish at once applied to the cover (the edge having been smeared with petroleum previous to the test). The cover, being held tightly in place with a broad elastic band, is immersed in a bath of water in a small open pan, kept at constant temperature (98 F.). At intervals the dish is removed from the water-bath and the drops inspected without removing the lid. Coagulation is considered to be complete when the profile of the drops does not change as the dish is tipped vertically and when the drops show an evenly distributed density by transmitted light. (For full description see original article.)

In the hands of Solis-Cohen, this method gives an average clotting time for adults' blood of $8\frac{2}{3}$ minutes.

With a little practice the method affords an easy and rapidly executed determination, and, in so far, seems to be free from criticism. Its disadvantage lies in the fact that there is not even approximate uniformity in the diameter and especially the depth of the drops. It is not feasible accurately to time and observe the clotting of more than four drops during one test. Among these four, the disparity in size may be quite marked. Although Solis-Cohen concludes that drops of a diameter between 4 and 7 mm. clot with equal rapidity, we have been unable to confirm his findings.

For this reason we have had constructed four smooth glass disks 5 mm. in diameter, which were cemented to the lid of the stender-dish. The drops were then collected on these disks, which insured reasonable uniformity in the diameter of each. This method, being an adaptation of Duke's technic, we called the Solis-Cohen-Duke.

In spite of the uniformity in diameter, however, it was found to be impossible to secure drops of equal depth. The importance of the depth in determining the rapidity of clotting may be seen from the following:

Average coagulation-time of drops in 29 tests: Deep, 13.5 minutes; medium deep, 10.3 minutes; shallow, 6.5 minutes.

The clotting time for one drop, so large as barely to adhere to the disk, was twenty-one minutes (not included in making the averages above).

In both the original and modified Solis-Cohen methods, the chief inherent factors of error will be found, therefore, in the size and depth of the drops, and, although practice may minimize the error, it seemed desirable to avoid it.

With this difficulty emphasized, the method of collecting blood on fine wire loops of uniform size fastened to a wire stem offered distinct advantages.

The chief objection which has been raised to this method originated by Biffi, is that contact of the blood with the wire loops hastens coagulation and that fibrin is attracted by capillarity to the point at which the loop touches the stem.

In his use of the instrument, Addis found that whenever the wire touched the water the blood in all the loops became diluted. In the apparatus which we used (see below) this difficulty was never encountered.

It has been claimed, also, that the loops are not so easily cleansed as glass. This is clearly unwarranted, since heating in the live flame is an ideal method of securing absolute cleanliness.

The original instrument used by Biffi consisted of a glass jar with a cork perforated for the passage of the fine platinum rod with its five loops attached, and for a thermometer. The latter registered the temperature of water contained in the lower part of the jar. When the loops are filled with blood the rod is passed at once through the cork into the warm moist chamber over the water. At stated intervals the rod is pushed down until one after the other of the loops is introduced into the water. Coagulation is complete when the blood remains on the loop instead of being diffused into the water.

From the theoretical standpoint, it would seem that coagulation would be hastened by contact with wire. Reference to Solis-Cohen's table, however, shows that the clotting time by Biffi's method is from seven to ten minutes, which is a fair average of all the methods and distinctly longer

than is obtained with the use of capillary tubes. The maximum-minimum range also is not so great as is seen in other methods.

Finally, it must be noted that the results with the Biffi instrument should be as uniform as those with any other, and permit, therefore, of a fair comparison.

In using the original instrument, difficulty was encountered in maintaining the proper temperature owing to radiation through the glass. In order to correct this defect, Brooks modified the instrument without altering the principle.

DESCRIPTION AND TECHNIC

The Biffi-Brooks coagulometer (Figure 1) consists of a movable glass tube 2.5 cm. in diameter, set in an oblong metal water-jacket, which surrounds three-quarters of the circumference of the tube. The metal cap of the glass tube contains two openings, one for a thermometer, the other for a metal rod on which is fitted a platinum wire 6 cm. in length. Beginning at the distal end of this single wire, four circular loops are made, 6 mm. apart, each 3 mm. in diameter.

We have added to the instrument a collar on which the metal cap of the glass tube lightly rests, facilitating its removal. Originally the caps fitted the tube so tightly as to make its removal too difficult for delicate work. We also replaced the screw-cap of the water-jacket with a thermometer, held in position by a rubber washer, thereby securing better control of the temperature in the water-jacket. Finally, we covered the water-jacket on three sides and bottom with asbestos, to prevent too rapid heat radiation.

In using the apparatus the water jacket is filled with water at 98 to 100 F. and the glass tube is slightly less than half filled with water at 98 to 99 F., which temperature must be maintained throughout each examination.

In perfecting our technic with the Biffi-Brooks instrument, much time was spent and many examinations were made which cannot be included in the tabulated results.

We finally selected the following course of procedure: The blood was obtained from a finger, since it was found to be much easier to control than any other locality. First, the wire loops were cleaned in the flame of an alcohol lamp. The skin of the finger was washed with tincture of green soap and distilled water and then with 95 per cent. alcohol. Puncture was made deep enough to permit the free flow of blood. The first drop was wiped off with a dry cotton pledget, and then the distal loop filled from the second drop, care being taken not to touch the skin. The excess blood was then wiped off, and the second loop filled from the third drop; the third loop from the fourth drop, etc. The only variable factor is the thickness of the film of blood in each loop. Since small drops permit of securing too thin a film, care should be taken to secure a large free-flowing drop.

When all the loops were filled, the rod was at once introduced into the warm air chamber above the water in the glass tube. Within a definite time after the puncture of the skin—usually four to five minutes—the rod was gently lowered

until the distal loop entered the water. Coagulation was considered to be complete only when the structure of the clot within the loop remained intact. It frequently happened that a very small amount of pigment would dissolve out of the coagulum.

There seems to be slight doubt that such solution of a minimal amount of pigment could not be interpreted as incomplete clotting so long as the loop was completely filled by a firm fibrinous clot. We have regarded such cases as "positive," therefore, in tabulating our results.

In a private communication from Harlow Brooks, he states that he has been accustomed to accept the appearance of fibrin shreds within the loop as an indication of coagulation. Such an assumption seems to us hardly justified since the presence of a small amount of fibrin by no means insures that firm and definite clotting has occurred. On the other hand, a clot in the loops, of toughness sufficient to withstand the solvent action of water, must give evidence of an ample supply of all the factors concerned in clot formation. For example, it has been shown that the clotting-time in certain cases of purpura may be within normal limits although the clot itself is soft and gelatinous, without tendency to contract. This condition has been supposed to be due to deficiency in one of the before-mentioned elements, possibly the prothrombin. It would seem to us, therefore, that the test as we have accepted it, furnishes a clue not only to coagulation *per se*, but also to the integrity of the resulting coagulum.

It is only fair to state, however, that we found certain discrepancies, the explanation of which is not certain. They can be shown in the following classification:

Coagulation complete in distal loop, not in the others, at same time, 6 examinations.

Coagulation greater in distal loop than in any others, at same time, 11 examinations.

Coagulation greater in first and second loops than in any others, at same time, 2 examinations.

Coagulation greater in first, second and third than in fourth at same time, 1 examination.

Coagulation incomplete in first, third and fourth, but complete in second at same time, 3 examinations.

In another case the third loop failed to show as much coagulation as the second at the same time.

Such inconsistencies probably depend on several factors.

It would seem to us that proximity of the blood to the warm water in the glass tube probably plays the most important rôle.

At the beginning of our work, when we were experimenting with technic, we found, in filling the proximal loop first, a number of instances in which the *distal* loop, nearest the water, showed the most advanced coagulation. Another factor is the possible variation in the thickness of the film of blood in the different loops. Of least importance, probably, is the factor of time — the distal loop being the first one to be filled.

The premature coagulation in the distal loop is less of an objection than may be supposed, because this loop is usually sacrificed in order to determine how rapidly coagulation is proceeding. When the first loop is found to be firmly coagulated the next loop is introduced at once, and the further procedure is determined by the effect of the water on the blood in it.

Two other objections, however, can be found against the instrument which are more serious.

The chief difficulty encountered is the inability to determine the end-point at every observation. All of the loops may be lowered into the water without the completion of coagulation in the last, thereby necessitating a second puncture. This is a more or less serious objection in the case of a struggling child. With increasing familiarity with the appearance of each loop as it was immersed, the number of failures to allow time for complete coagulation grew less, so that we determined to continue the use of the instrument because of its manifest advantages in securing greater uniformity in size of the drops and because of the ease and rapidity of technic.

The second objection is that four loops do not permit of frequent tests for coagulation and the time must often be reckoned in minutes instead of half and quarter minutes.

With practice, however, one learns to judge quite accurately from the behavior of the blood in one loop when to introduce the next. A five-loop rod, such as Biffi advised, would also increase the scope of the instrument. Finally, it is questionable whether shorter intervals than one minute offer any advantage in procedures which are more or less inaccurate, as are all of these clinical methods.

Our clinical material has been drawn from the Children's Departments of the Philadelphia General, University and Presbyterian hospitals and the Children's Hospital.

We have made 192 examinations of 176 patients. Of these, eighteen examinations of sixteen patients gave an undetermined coagulation time, and re-examinations could not be made. (In ten other examinations

coagulation time could not be determined at first, but re-examinations gave positive results. Only the positive results, therefore, have been considered in our tables.)

Of the 160 patients who gave a positive coagulation time, thirty-five were healthy, without ascertainable disease, except such affections as ring-worm of the scalp and scabies (eight cases); 125 patients suffered from a variety of diseases which will be detailed later. Grouping all the healthy cases and all those suffering from disease, we find the following averages:

Healthy Cases: Average coagulation time, 39 examinations, 9.4 min. (5-14 min.).

Cases not Healthy: Average coagulation time, 135 examinations, 9.7 min (5-16 min.).

This shows an unimportant difference between the well and sick.

It is obvious that the cases which failed to give positive results are difficult to interpret. It is also obvious that they should not be excluded, and that any series in which one or more of them occur cannot be considered conclusive.

In order to make some use of them we have made the following calculations:

In eighteen examinations of sixteen patients, complete coagulation did not occur within an average time of 10.9 minutes.

Grouping the positive cases, both healthy and diseased, we find that 160 patients give an average coagulation time of 9.6 minutes (174 examinations).

Since the positive cases (160) exceed the undetermined cases (sixteen), as 10 is to 1, and the average coagulation time of the latter certainly exceeds that of the former by at least 1.3 minutes (80 seconds) —(10.9 to 9.6 minutes)—it will be seen that the average of positive cases should be increased by a minimum of one-eleventh of the difference between positive and negative. This would be approximately seven seconds or .13 of a minute.

Since we cannot tell how much more than the minimum should be added, we may express the combined figures with a plus sign, thus:

Blood of 176 patients gave an average coagulation time of 9.73 minutes + (192 examinations).

Although even by this calculation, the results cannot be considered accurate the error must be slight since we found, in the ten "negative" cases which were re-examined, the positive time for coagulation as often

less, as it was greater, than the "negative" time. In other words, the blood which failed to coagulate within twelve minutes one day, might show a positive result in eleven minutes or thirteen minutes the next day.

In order to compare the results of tests made by the Biffi-Brooks method with those which we obtained by the Solis-Cohen method, the following figures are presented:

Solis-Cohen Method: Forty-one cases gave an average coagulation time of 7.6 minutes (5-11) (fifty examinations).

The shorter time observed in the Solis-Cohen method is easily accounted for by the more stringent proof of coagulation which is demanded in the Biffi-Brooks method, and would seem to dispose of the claim that the use of wire-loops materially hastens coagulation.

In order to determine the influence of other factors on the coagulation time, we made further subdivisions of our cases tested by the Biffi-Brooks method. Since we found no material difference in total averages between well and sick children, we can disregard the influence of disease in formulating the accompanying tables:

TABLE 2.—COAGULATION TIME, CONSIDERING AGE, SEX AND COLOR

			Results	
Age—	Time		Positive	Negative
From birth to 2 years	9.0 min.	+	34	2
Third to seventh years inclusive	9.8 min.	+	68	16
Eighth to fifteenth years inclusive	10.3 min.		72	..
Sex—				
Males gave an average coagulation time of	8.5 min.	+	102	10
Females gave an average coagulation time	9.7 min.	+	72	8
Color—				
White children gave an average coagulation time of	9.1 min.	+	142	11
Colored children gave an average coagulation time of	9.7 min.	+	32	7

The figures for age will be discussed later. Those for sex show a greater difference than is found by Rudolf, who gives 7.76 minutes and 7.54 minutes, respectively, for males and females.

According to our results, there is no noticeable difference between the white and colored races in the early years of life.

We have made no attempt to determine those differences which depend on the time of day, according to the published reports of other observers.

In view of the great variations found in the blood of the same patient within a few minutes, it seems to us that the limitations of the clinical method would preclude the possibility of drawing trustworthy conclusions

on this point. For the same reasons the influence of the ingestion of food or fluids, of exercise and of fever on coagulation time have been disregarded.

As has been said, we have had no case of hemorrhagic disease to examine other than that of scurvy. Likewise cases of hemorrhage, urticaria, severe anemia, leukemia, etc., have not been observed in our series.

There remains, therefore, the consideration of the effect of a variety of diseases on coagulation time (Table 3).

It is clear that the number of cases in most of the classes examined is too small to permit of drawing conclusions. The figures, therefore, are presented merely to be of record.

TABLE 3.—SHOWING EFFECT OF A VARIETY OF DISEASES ON COAGULATION TIME

DISEASES IN WHICH POSITIVE DETERMINATIONS WERE OBTAINED

Disease	Cases	Number of Examinations	Average Coagulation Time, Minutes	Minimum and Maximum, Minutes
Rubella (eruptive stage)	3	3	11.3	8 -16
Pertussis (paroxysmal stage)	3	4	9.4	6.5-13
Typhoid fever (febrile stage, one in relapse)	3	4	8.9	7 -11
Syphilis (hereditary)	4	4	8.9	7 -11
Chorea (one acute, two convalescing)	3	3	12.0	10 -14
Vaginitis (acute)	3	3	9.6	6 -13
Valvular heart disease (afebrile compensated)	5	5	8.4	5 -14
Infantile paralysis (chronic stage)	5	5	8.6	7 -11
Bronchitis (acute or subacute)	4	4	9.1	6 -11
Bronchopneumonia (uncomplicated) (4 acute, 7 convalescing cases)	11	11	8.9	6 -12
Bronchopneumonia (complicated) (acute stage) Four cases occurred with measles, and one with varicella. Since these diseases show a lengthened coagulation time they may be grouped	5	6	10.5	9 -12
Bronchopneumonia (complicated) (acute stage) Two cases occurred with pertussis, one with typhoid and one with vaginitis. Since these diseases show a normal coagulation time they may be grouped	4	4	8.0	5 -10
Combining all the results in bronchopneumonia, we find	20	21	9.2	5 -12
Tuberculosis,* Class 1: 11 active, 8 quiescent	19	22	11.5	9 -14

*We have divided the cases of tuberculosis into two classes: (1) Tuberculosis of the bones, joints, glands or skin, and (2) tuberculosis of the lungs, peritoneum, kidney, or general. Only those cases were included in which a diagnosis was absolutely justified. Several of the cases of rickets probably belong to this class, but the diagnosis could not be definitely established. Tuberculosis cases (Class 2) and certain other diseases containing some negative results are grouped together later.

TABLE 3.—*Continued*

INDIVIDUAL CASES OF VARIOUS OTHER DISEASES

Disease	Cases	Number of Examinations	Average Coagulation Time, Minutes	Minimum and Maximum, Minutes
Cerebrospinal meningitis (height of the disease)	1	..	5.0	.... ..
Scurvy (postorbital hemorrhage) (infant 10 months old)	1	2	5.75	5.5- 6
Nephritis with ascites	1	..	15.0	.....
Cretinism (taking thyroid extract for 6 years more or less continuously)	1	..	6.5	.....
Erysipelas	..	..	9.0	.....
Metastatic abscess	..	..	8.0	.....
Epiphysitis	..	..	6.5	.....
Cervical adenitis	..	..	9.0	.....
Cystitis	..	..	10.0	.....
Favus	..	..	10.0	.....
Empyema (2 examinations)	..	..	14.5	.....
Cerebral paralysis of arm	..	..	13.0	.....
Multiple neuritis	..	..	13.0	.....
Club-foot (much crippled)	..	..	12.5	.....
Congenital dislocation of hips (in bed)	..	..	12.5	.....

CASES GIVING BOTH POSITIVE AND NEGATIVE RESULTS

Tuberculosis, Class 2: 8 active cases—lungs, peritoneum, kidneys or general‡	8	10	11.7+	9-14+
Measles (eruptive stage) 10 positive, 3 "negative" results	12	13	9.5+	5-12
Varicella (eruptive stage)	4	4	11.8+	10-14
Croupous pneumonia (4 acute, 2 convalescing)	6	6	7.4+	5-10
Infantile atrophy	5	5	9.0+	6-12+
Rachitis	9	9	10.3+	6-12

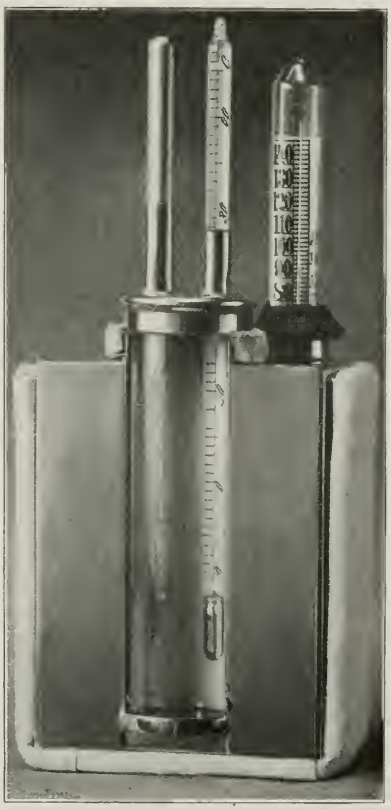
From the results in a few diseases, however, it would be permissible to draw inferences.

Taking the average coagulation time of normal blood in childhood as 9.5 minutes (Biffi-Brooks method), we find that bronchopneumonia, which gives an average of 8.9 minutes uncomplicated, or 9.2 for all cases, seems to exert no material influence on the coagulation time. According to Solis-Cohen, there is no uniformity in results with adults' blood in this disease, both a lengthened and shortened time having been found. In lobar pneumonia Rudolf and Cole found an average of 8.1 minutes in forty-seven observations on seventeen cases, Rudolf's average for normal children being 8.04 minutes.

‡One case showed no coagulation at the end of thirteen minutes.

Our figure of 7.4 + minutes for lobar pneumonia cannot be of much value for comparison, because it is based on so few observations.

Rudolf and Cole found an average coagulation time of 7.1 minutes (5-12 min.) in sixty observations on twenty-six cases of typhoid fever in children. This shows a greater reduction in coagulation time than we observed in our small number of cases (8.7 min., compared with 9.5 min. for normal cases).



Biffi-Brooks coagulometer as modified by the authors. For description see text.

In measles, the coagulation time was approximately normal (9.5 + min.). In tuberculosis, on the other hand, we found the most distinct change (Class 1, 11.5 min., Class 2, 11.7 + min.) of any — the difference between normal and diseased cases amounting to more than two minutes.

If we were to take a positive von Pirquet reaction as a criterion for diagnosis of tuberculosis, this disparity might be increased, since several of the cases of rachitis which gave a lengthened coagulation time, would then have been included in the tuberculous class. We have, however, made the determination of tuberculosis depend on evidence of active, or very recently active, lesions.

Solis-Cohen and Vierordt found a shortened coagulation time in the blood of tuberculous adults, while Addis' results were the same as in normal cases. In no other class of disease did we find such uniform results as in tuberculosis, practically all of the cases showing a decided delay in coagulation.

The very short coagulation time in the one case of meningococcus meningitis (5 min.) and the lengthened time in nephritis with edema (15 min.) would be of greater interest were it not for the fact that these limits — five minutes and fifteen minutes — are not especially unusual for any class of cases. On the other hand, the one case in which we would expect to find a lengthened coagulation time (scurvy) gave a relatively short result (5.75 min.—two examinations).

Although the literature contains very little reference to the coagulation time in childhood as compared with adult life, the usual statement we find is to the effect that there is practically no difference except during the first few days of life, when a delay is observed.

Our results for older infants and children show no material differences from the accepted results, although the average for childhood is slightly higher than the average for adults tested by the Biffi method. (Authors, 9.5 min., Biffi, 7-10 min.)

Literature based on Biffi's original method or on the Brook's modification, contains nothing for comparison with children.

A study of our own and published results, according to various methods, emphasizes certain facts. *First*, that in each individual disease the maximum and minimum figures usually show a wide variation. We have alluded to this in referring to our figures for meningitis and nephritis. It is easy to see that the possibility of such variation in a selected case would be apt to negative the importance of the result. For example, in our normal cases, we find a range of from five to fourteen minutes. Either figure by itself shows a far greater variation from normal than the *average* figure for any kind of disease in our classification.

In the same way Rudolf, using his own method,[1] found a variation of from five to twelve minutes in typhoid fever. (His limits in normal cases are not published.) Such variation, in spite of the utmost care and skill after long practice, seems to prove that the clinical method — at least that one not dependent on complicated apparatus — fails to indicate any but the most gross changes in coagulation time.

The *second* noteworthy fact is that the various diseases show *average* differences which can hardly be considered of any real importance, especially in view of the before-mentioned variation in the individual case. We would emphasize the importance of the fact that the *average* figures show much less variation than those for the *individual.*

Finally, we find rather more than the usual disagreement in the results of various observers. Allowing for the personal factor and the difference in technic and method, the inconsistencies still appear to be unduly conspicuous.

If these objections be true in regard to the results in adults, our work has proved them to be equally true in the case of the child, with the added disadvantage that the examinations of coagulability of blood in children are attended with increased difficulty.

It would seem to us that future efforts should be directed toward solving the problem of blood coagulation *per se,* or to a study of coagulability according to the more advanced standards, i. e., the determination of the presence or absence, increase or diminution, in one or more of the various elements concerned in the formation of thrombin and in the latter's action on fibrinogen.

It seems to us very improbable that any important variation exists in the mere time of coagulation of the blood in diseases other than of so-called hemorrhagic type. This opinion may be equalified by the statement that *average* differences of one, two or three minutes can hardly be construed as of any practical importance, especially when we consider the limitations and variations of the great majority of the so-called clinical methods. The chief value of the latter may be for comparison, yet, even in this case, the results must be interpreted with caution since the normal variation often is so great.

Of much more importance is the determination of the firmness and texture of the clot. For this reason it would seem that immersion in water is a more rigid test than that applied by most of the other clinical

1. Rudolf fills a capillary tube with blood and observes the formation of fibrin by breaking off sections of the tube at regular intervals.

methods and to this extent, at least, the method originated by Biffi presents distinct and practical advantages.

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DISCUSSION

DR. HAND asked if any such studies had been made in cases of typhoid fever and pneumonia. In both these diseases there was quite a considerable formation of fibrin which caused a more or less plastic state of the blood; this might explain the beneficial effects from the drugs used in lessening the plastic state of the blood.

DR. GRIFFITH emphasized the value of the investigations reported by the writers of the paper. He asked Dr. Carpenter whether he could determine, as a result of his studies, if any importance should be attached to the study of the coagulability as an indication for or against operation in cases of adenoid growths. He knew that some specialists laid stress on such examination, but said that he himself had always felt rather skeptical about the value of this.

DR. CARPENTER, closing the discussion, said that they had found the coagulation time of the blood in cases of bronchopneumonia to be practically normal. The cases of lobar pneumonia had given a shorter coagulation time, but it would be a mistake to attempt to draw any definite conclusions from a report on such a limited number of cases. There were more cases of bronchopneumonia examined than of lobar pneumonia. In answer to Dr. Griffith he did not believe that the estimation of the coagulation time by the clinical methods at present employed was of much practical use except where a decided delay in the coagulation time was demonstrable.

INCLUSION BODIES IN SCARLET FEVER BLOOD AS A MEANS OF DIFFERENTIAL DIAGNOSIS*

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In the *Centralblatt für Bakteriologie* of November, 1911, Professor Döhle,[1] of the Institute of Pathology of Kiel, reported that he had found in the blood of some 30 cases of scarlet fever which had been sent to him certain inclusion bodies, mainly in the polymorphonuclear leukocytes which, to his knowledge, had not been previously described. In a large number of controls, the nature of which was not stated, he found similar bodies only in a case of pneumonia, which may, however, have been mislabelled, and in 2 cases of carcinoma, in one of which they were not typical; the second case was also a luetic. Dr. Martin Kretchmer,[2] of Strassburg, reported, in the *Berliner Klinische Wochenschrift* of March 11, that he had been able to confirm these observations after examining an equal number of scarlet fever cases. He also examined 70 controls, among which were 20 normal bloods, together with cases of measles, diphtheria, tuberculosis and syphilis. The bodies were found in 1 case of pneumonia with abscess of the neck, in 2 cases of empyema of streptococcus origin following diphtheria, and in 1 of 9 cases of tuberculosis. He was not able to find them in 6 cases of carcinoma, or in an equal number of syphilitic cases. He suggests the possibility of streptococcus infection being the cause of these bodies. Neither of these writers was able to find the bodies in animals before or after inoculation with scarlet fever blood. In April, in collaboration with Dr. Anna W. Williams,[3] I presented to the Pediatric Section of the Academy of Medicine, the results of work performed at the Research Laboratory of the Department of Health on this subject. This has now been carried further, so that I am able to report the results of examination of some 115 cases of scarlet fever blood, and of about 80 controls. In selecting the latter, little effort has been made to determine the prevalence in general of these bodies, but realizing that, in all probability, they would prove of practical rather

* From the Research Laboratory, Department of Health, New York

1. Döhle, Prof.: Centralbl. f. Bakteriol., Orig., lxi, Part ½.
2. Kretschmer, Martin: Berlin Klin. Wchnschr., March 11, 1912, No. 11, p. 49.
3. Nicoll and Williams: Arch. of Pediat., May, 1912, xxix, No. 5.

than scientific value, blood has been taken, in so far as possible, from such pathologic conditions, as the clinician is frequently required to differentiate from scarlet fever.

To those of you who have not seen the reports referred to, I would say that these bodies are readily brought out by a number of stains, of which I may mention those of Giemsa, either used immediately or left over night; of Pappenheim and of Manson (borax, methyl blue). The latter for practical purposes is far superior to the others mentioned and fulfills all requirements of diagnosis. With it the red blood cells take

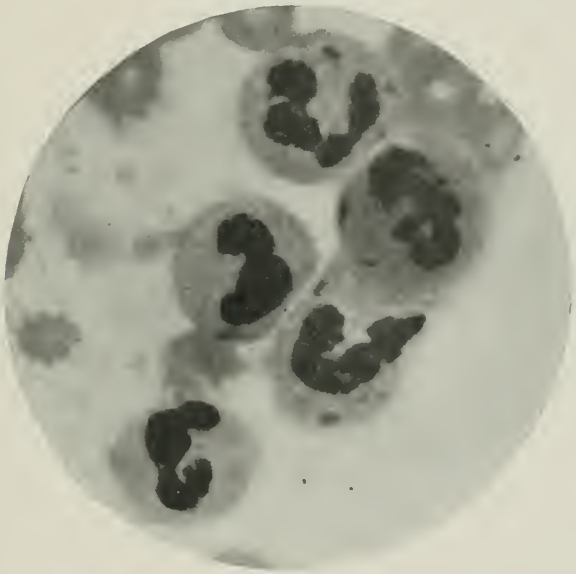

Fig. 1.—Blood from two cases of scarlet fever taken the fourth day. The inclusions are seen in the leukocytes less deeply stained than the nucleus. (Manson's stain.*)

on a bluish green tinge, the nuclei of the leukocytes a very deep blue, the cytoplasm a very faint blue, and the inclusions a shade somewhat between the two. The latter are of various sizes and shapes; coccus formed, long and narrow masses, and often irregular splashes of blue of large size. In fresh cases of scarlet fever they are found in nearly all the polymorpho-

*I am indebted to Prof. Francis Wood, of Columbia University, for the excellent photographs herewith produced.

nuclear cells, varying in number from one to six or more. Contrary to the observations of Kretchmer, a prolongation of the fever and symptoms beyond the usual time is very apt to result in a longer duration of the bodies in the blood, which, in average cases, tend to disappear after the first week of the disease and sometimes before. Of the 115 cases, 100 were taken from the scarlet fever wards, the remaining being sent from other hospitals or physicians for differential diagnosis. The great majority of the patients had been ill from one to seven days. They represented all types of the disease, from the very mildest to the most

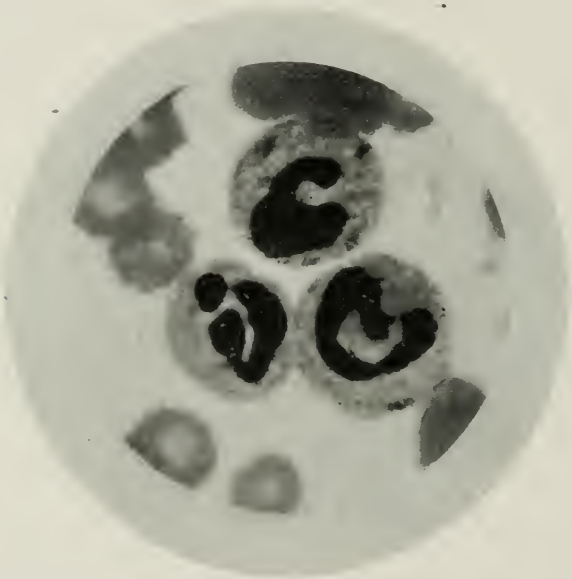

Fig. 2.—Blood from two cases of scarlet fever taken the fourth day. The inclusions are seen in the leukocytes less deeply stained than the nucleus. (Manson's stain.)

severe. In this series but 16 failed to show the inclusion bodies. One of these had been ill for four days, and although it was sent to the Scarlet Fever Hospital the diagnosis seemed to me to be by no means certain. Two other cases of five days' duration of undoubted scarlet fever also failed to show the bodies. The other negatives, with one exception, had been ill from seven to twenty-eight days. The exception referred to was that of a child of six who was attacked with a fulminating type of scarlet fever, fortunately very rarely seen; was admitted to the hospital

with a temperature of 106 F., twelve hours after the onset of the disease, and who died twelve hours later, with a temperature of over 107 F. The rash consisted of a dull bluish mottling. The blood showed hardly any leukocytes, and these contained no inclusion bodies.

I have divided the controls for practical reasons into those cases which would not be clinically confused with scarlet fever and those which are frequently so. The bodies were not found in normal blood. In six cases of syphilis examined, giving a positive Wassermann reaction, they were found in one, that of a man admitted to the diphtheria hospital with an

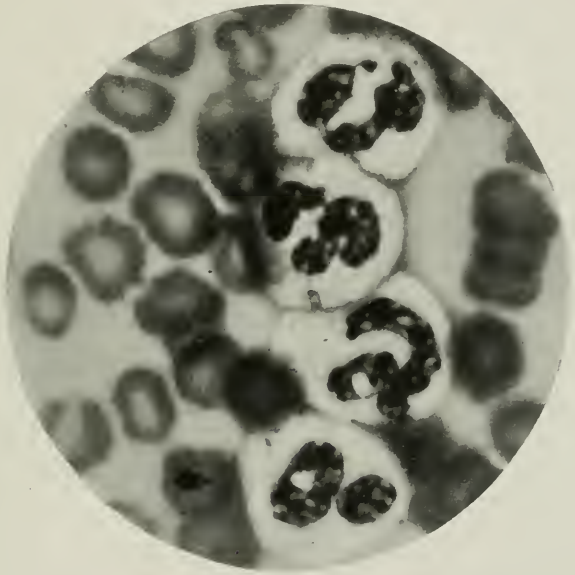

Fig. 3.—Blood from two cases of scarlet fever taken the fourth day. The inclusions are seen in the leukocytes less deeply stained than the nucleus. Manson's stain.)

intensely red throat, cultures from which were negative for diphtheria. He had been luetic for five months only, and the condition of the throat was probably due to syphilis and an acute invasion of streptococcus.

Eight cases of erysipelas all showed inclusion bodies. Three cases of diphtheria were negative. Three diphtherias complicated with pneumonia were negative. One case of general lymphatic hypertrophy of unknown origin in a child was negative. One case of varicella was negative. Two cases of uncomplicated whooping-cough were negative

One case of empyema was positive. One case of acute tuberculous pharyngitis was negative. Four cases of typhus fever were positive. Of control cases possible to confuse with scarlet fever, twenty-three measles proved negative. Seventeen cases of German measles proved negative. Three follicular tonsillitis, negative. One case of dermatitis exfoliativa negative. Twelve antitoxin rashes of various types all negative. Two cases of rash, probably following intestinal toxemia in infants, negative, while seven cases of sepsis, most of them of puerperal origin with and without rashes, proved typically positive.

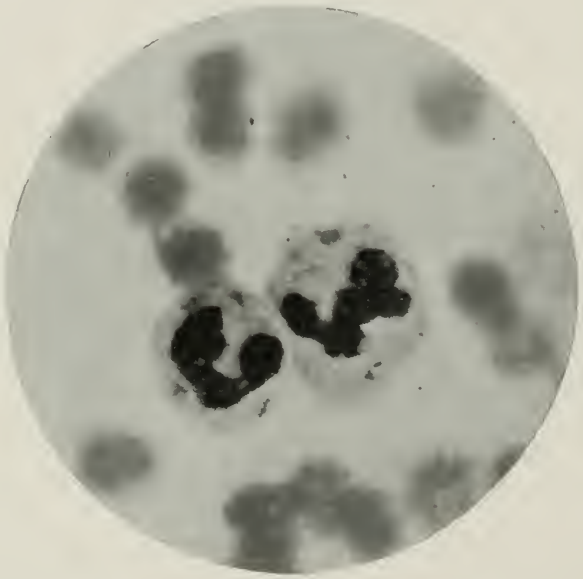

Fig. 4.—Blood from two cases of scarlet fever taken the fourth day. The inclusions are seen in the leukocytes less deeply stained than the nucleus. (Manson's stain.)

It is to be noted that the number of cases of tonsillitis is too few from which to draw positive conclusions, and as this condition not infrequently is confused with scarlet fever, especially when the former is accompanied by a rash, a further examination of tonsillitis cases is very desirable. From this series of observations, it is possible to judge of the value, as well as the limitations of this method of diagnosis, and I believe that we are justified in stating that these bodies will be found in every case of scarlet fever with the exception of the fulminating type, who die

before the tissues have time to react, up to and including the fourth day of the disease, that they will not be found in antitoxin rashes, measles, German measles, various toxic rashes due to drugs, to intestinal absorption, probably not in ordinary tonsillitis, but regularly in general sepsis, for which reason, unfortunately, the latter condition so frequently confused with scarlet fever cannot be distinguished from it by the blood examination. During the past month this method of diagnosis has been put to practical use at the hospitals of the Department of Health as well as among patients of private practitioners who have sent blood for diagnosis, and we have thus been able to make correct diagnosis in serum rashes, mistaken for scarlet fever and the reverse, German measles with scarlatinaform rashes, and various other obscure conditions, and as far as could be determined by the subsequent outcome of the case, the microscopic findings tallied with the clinical course in every instance. In practically all cases sent for purposes of diagnosis, the examiner of the blood smear was unacquainted with the clinical history until after an opinion had been expressed as to whether or not it was scarlet fever.

Technique.—For a satisfactory examination of the blood smears, it is quite essential to take a small drop of blood and spread it out evenly and thinly so that the leukocytes will not be distorted or cramped between red blood-cells or groups of other polymorphonuclears or pushed or pulled to the edge of the smear, but lie flat and by themselves. The smear is fixed in methyl alcohol, and thoroughly washed, then stained with Manson's stain, for ten seconds to half a minute. Again thoroughly washed and examined with the oil immersion. After a short experience the normal granules of the cell cannot be confused with the bodies under discussion, and not the slightest difficulty is found in recognizing the latter.

In conclusion, it would seem more than probable that the inclusion bodies may be expected to be present in the majority, at least of pathologic conditions, in which pyogenic organisms have produced an acute leukocytosis. In the cases of typhus fever there was a marked leukocytosis, and the throats of the patients were quite as red as those seen in scarlet fever. It would seem that we have in the blood examination of suspected scarlet fever cases an extremely valuable method of differential diagnosis between this disease and nearly all the conditions which resemble it.

DISCUSSION

DR. KERLEY said that a few weeks ago, on the same day, two children came down with a rash like scarlet fever but very atypical. He knew of the work Dr. Nicoll was doing and he sent two slides with the request that he tell him if they were

cases of scarlet fever. One slide was reported positive, the other negative. In the case which was reported as positive, the rash disappeared in a day or two; this child was in quarantine seven weeks and desquamated freely. The child that was reported as negative was in quarantine ten days and did not desquamate. Such observations as Dr. Nicoll had given were of a great deal of assistance in helping to differentiate obscure cases of rash when it was impossible to tell from a clinical standpoint whether a case was one of scarlet fever or a rash similating scarlet fever of other origin.

DR. BUTTERWORTH said that twelve years ago he was interested in yellow fever and, following an outbreak, he was sent to Vera Cruz to study the matter. He worked there three months studying the blood of those afflicted and believed that he had found a body which promised to throw much light on the subject. He published an account of it in *The Journal of the American Medical Association.* He then had to back water, for what he found was only yeast fungi. Therefore, he advised that they all go slow in these matters, such as presented by Dr. Nicoll.

DR. NICOLL said that they had not made an attempt to see how long the bodies would be found in a given case, but they did disappear in from five to twenty-eight days. With regard to Dr. Butterworth's observations, Dr. Nicoll did not really know what he meant. The bodies were there; they were not found in any other condition resembling scarlet fever so far as he knew, except in cases of sepsis. Just what these bodies were he did not know. Their nature had no bearing on their value as a means of differential diagnosis.

CONGENITAL OBSTRUCTION OF THE POSTERIOR URETHRA: REPORT OF A CASE IN A BOY AGED FIVE YEARS*

J. H. MASON KNOX, JR., M.D., AND T. P. SPRUNT, M.D.
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Urethral obstruction to the urinary flow may be brought about by a number of conditions. They are for the most part the result of inflammatory processes in the urethra itself, or of pressure on its lumen by the growth of surrounding structures, notably in prostate hypertrophy.

These changes acquired after birth are of frequent occurrence and are to be sharply distinguished from obstruction of the urethra present, although perhaps unrecognized, at the time of birth.

Without other reference to the interference with the urinary flow from gross malformation of the genito-urinary tract, and to the stricture of the urethra due to occlusion or narrowing of its external orifice, or of the pars navicularis, we wish to report an instance of a form of congenital membranous obstruction occurring in the prostatic portion of the urethra, because apparently this condition has not attracted the attention, at least in this country, that it deserves, and it may be that cases which might be relieved are not recognized.

CASE REPORT

History.—The case reported concerned a boy, F. S., aged 5 years. His family history was good; his father and mother were living, five brothers and four sisters were alive and well, and had no symptoms similar to those of the patient. The birth was normal. From infancy it was noted that there was frequency of micturition. It was necessary for the patient always to wear napkins, which were wet, according to the mother's statement, "about every half hour." The urine was described as often being "thick and milk-like." Otherwise the patient's life was uneventful until 3 years of age, when he had measles. Following this illness the patient seemed susceptible to colds and had much of the time a purulent discharge from the left ear.

He first came under the observation of one of us on June 26, 1911, when at the age of 4 years, he was admitted to The Thomas Wilson Sanitarium complaining of loss of weight and strength and moderate diarrhea.

Examination.—On examination the boy was found to be sparely nourished, pale and with evidences of rickets—marked Harrison's grooves and a moderate rosary.

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*From The Thomas Wilson Sanitarium and the Medical and Pathological Departments of Johns Hopkins Hospital.

His weight was 23 pounds. The lungs and heart were normal. The abdomen was considerably distended and pendant.

On palpation in the left lumbar region there was made out a soft movable lobulated mass extending from the anterior superior spine to the costal margin and to about midway between the umbilicus and the lateral border of the abdomen. This mass could readily be brought between the fingers in bimanual palpation; its borders were rounded and it was a little sensitive on pressure and dull on percussion. On the right flank a similar smaller mass could be made out emerging from the lower border of the liver.

A third rounded mass was detected in the mid-line extending from the symphysis pubis to the level of the umbilicus. This was oval in shape and regular in outline, freely movable and suggested an enlarged urinary bladder.

The liver was readily palpable 3 cm. below the costal margin and was not tender. The spleen was not enlarged.

External genitalia were normal. The patient had no fever and there was no history of intestinal obstruction.

Urine examination was important. The urine was slightly turbid and of low sp. gr. (1,002 to 1,004) and acid in reaction. It contained but a trace of albumin and no sugar. On microscopical examination a large number of pus cells were found, a few epithelial cells and red blood corpuscles. There were no casts. The amount of urine collected for twelve hours was 350 c.c. No tubercle bacilli were found in a centrifuged specimen. An attempt was made to catheterize the patient but the external meatus was too small to admit the smallest catheter available. There seemed to be at that time little interference with the flow of urine; no vesicle tenesmus was noted and there was no undue sensitiveness over the bladder.

A von Pirquet skin test was negative.

The urinary findings suggested a cystitis or pyelitis. The presence of the lobulated tumors above described in the flanks made the diagnosis of congenital cystic kidneys a possibility.

No marked change was noted in the patient's condition for several days, after which the lateral masses became smaller and finally could hardly be detected. Their reduction in size was apparently associated with the more thorough emptying of the bowels, although during the time of observation of more than two weeks there had been a formed or semi-formed large stool every twenty-four hours. Slight variation in the size was noted from day to day also in the fluctuating mass above the symphysis pubis.

The child's general condition bettered. His appetite was good and he was discharged improved on July 13. The clinical diagnosis at the sanitarium was: Pyelitis, hypertrophy and dilatation of bladder, rickets, intestinal indigestion with distention and partial fecal impaction.

The patient was not seen again until January, 1912, an interval of more than five months.

At this time he came to the children's out-patient department, The Johns Hopkins Hospital. He looked pale and extremely ill. The history was that although he had not been strong he had had no acute illness until two weeks before, when there had developed a cough and abdominal pain. He had since that time become progressively worse.

He was admitted to the service of Dr. Barker, January 3. On examination the boy was much emaciated. The breath-sounds were harsh and accompanied by a few moist râles. The abdomen was distended and a number of soft masses thought to be intestinal coils were made out on palpation.

Above the symphysis and extending nearly to the umbilicus was the same oval mass before noted, apparently a distended bladder. The blood examination was as follows:

Red blood corpuscles	5,100,000
Leukocytes	11,000
Hemoglobin	70 per cent.

The urine contained a large number of pus cells and a trace of albumin.

There was a purulent discharge from each ear, a large abscess in the left tonsil and a mucopurulent exudate on both tonsils and the pharynx.

The Wassermann reaction was negative. The patient was given bismuth by mouth and the motility of the intestines determined by *x*-ray examinations.

The stomach appeared slightly distended. The motility of the small intestines seemed normal. The sigmoid flexure of the colon was displaced somewhat to the right and there seemed to be an unusual stasis between the sigmoid and the rectum.

This condition helped to account for the large lobulated mass in the left flank which gradually disappeared when the bowel was thoroughly evacuated. There was some phimosis and the patient was circumcised.

The child did not improve in the hospital. On several occasions acute dilatation of the stomach was noted and shortly before exitus on January 18, there were repeated convulsive spasms.

The temperature did not rise above 99 F., nor did the pulse exceed 120 to the minute.

PATHOLOGICAL FINDINGS

Necropsy (3670) was performed ten hours after death by Dr. Sprunt.

Anatomic Diagnosis.—Congenital malformation with obstruction of the prostatic urethra; dilatation and hypertrophy of the bladder and ureters: bilateral hydronephrosis; chronic posterior urethritis, cystitis, ureteritis and pyelitis: bilateral chronic suppurative otitis media: cloudy swelling of viscera; emaciation: unilateral congenital cystitic kidney: chronic pleural adhesions: operative scar of circumcision: acute anterior urethritis; adenoma of right adrenal.

The body is that of an emaciated male child, 80 cm. in length. There is no subcutaneous edema. The prepuce has been recently removed: otherwise the external genitalia seem normal on inspection and palpation.

After opening the abdominal cavity the viscera are found normally disposed, excepting the cecum, which lies in the left lower abdominal quadrant, is quite freely movable and can easily be brought back to its usual position. The bladder is very large and extends half way to the umbilicus. By firm pressure on the bladder a very small stream of urine can be expressed from the external meatus of the urethra. On following the sigmoid flexure into the pelvis it is thought at first that it turns on itself and runs back upward toward the right kidney, but after further dissection, this structure is found to be an enormously dilated and hypertrophied ureter of about the same size as the sigmoid flexure of the colon.

Examination of the brain and meninges reveals no abnormalities. Except for pleural adhesions on the right side and a mild grade of bronchitis, the thoracic viscera are normal. The heart weighs 70 gm.

The spleen, pancreas, stomach and liver show nothing noteworthy. The adrenals are normally placed. The medulla of the left adrenal is softened. About the center of the right adrenal there is an irregular thickening, roughly 1.5 cm. in diameter, which seems fused with the kidney capsule beneath it. It resembles

in general the adrenal cortex but with less regular markings and with rather coarse, white strands running through it.

The organs of the urinary system were carefully dissected and a sketch made of them *in situ* by Mr. J. P. Webster of the Johns Hopkins Medical School (Fig. 1). The kidneys are in their normal position and are both enlarged, but are not exactly alike. The larger size of the left kidney 9x4.25x3.5 cm., is only partly explained by the formalin injection of its ureter under slight pressure. On palpation the kidneys give a distinctly fluctuating sensation as if the organs were merely thick-walled sacs. The fetal lobulation is easily seen on both and on the surface of the smaller right kidney, 7x5x2.5 cm., there are several thin-walled cysts, the largest measuring 2 cm. in diameter. On longitudinal incision both kidneys consist of a mass of dilated cystic spaces, evidently the dilated calyces which are continuous with the ureter below. The whole thickness of the kidney parenchyma, from calyx to capsule, averages from 5 to 7 mm. with occasional thicker areas, measuring 15 mm. between the larger calyces. The structure of cortex and medulla cannot be distinguished. The blood-supply of the kidneys seems quite normal.

The ureters show the normal relationship to kidneys and vessels; they are very tortuous in their course but otherwise follow the normal path. They are greatly enlarged, of the same size, 1.5 cm. in diameter, and have firm, thick walls.

The bladder was opened longitudinally along its anterior wall while *in situ*. It measures 7 cm. in length from internal meatus to apex. There are scattered ecchymoses in the mucosa which is elsewhere quite pale. Beneath the mucosa the musculature is thrown up into very prominent trabeculae. The ureteral and urethral orifices are in their usual relative positions. A small probe is easily passed into the ureters from the bladder, but in the urethra meets with an obstruction in the lower prostatic portion. Similarly when the urethra is sounded through the external meatus, an obstruction is encountered in the same region. The whole urinary tract is then removed *en masse*, including half of the anterior urethra and opened along the anterior wall.

Through the wide internal meatus the bladder becomes continuous with the greatly dilated and thick walled prostatic urethra which forms an oval sac with the distal, blind extremity 2.5 cm. from the internal meatus. The floor of this pouch shows several prominent folds near the midline which end below in an unusually prominent verumontanum which reaches three-fifths of the distance from the internal meatus to the blind end of the sac. The opening of the vagina masculina is conspicuous, shaped like a crescent, with the concavity directed upward. Numerous orifices of the prostatic ducts are observed on each side of the verumontanum but those of the ejaculatory ducts are not seen. Immediately below the verumontanum, the ridge, of which it forms a part, divides into two prominent diverging folds which soon fuse with the anterior wall of the urethra instead of fading out gradually on the posterior wall of the membranous urethra as usual. Just below the verumontanum between the diverging folds, there is a small equilateral triangular opening whose sides measure about 3 mm. A probe passed through from the anterior urethra presents in this opening and abuts against the hypertrophied verumontanum. This is the only communication between the anterior and posterior portions of the urethra.

The mucosa of the dilated prostatic urethra is pale and resembles that of the bladder in appearance. The mucosa of all that portion of the urethra anterior to the obstruction is swollen, reddened and shows small ecchymoses.

The anus and rectum seem quite normal. Nothing unusual is noted about the seminal vesicles or vasa deferentia.

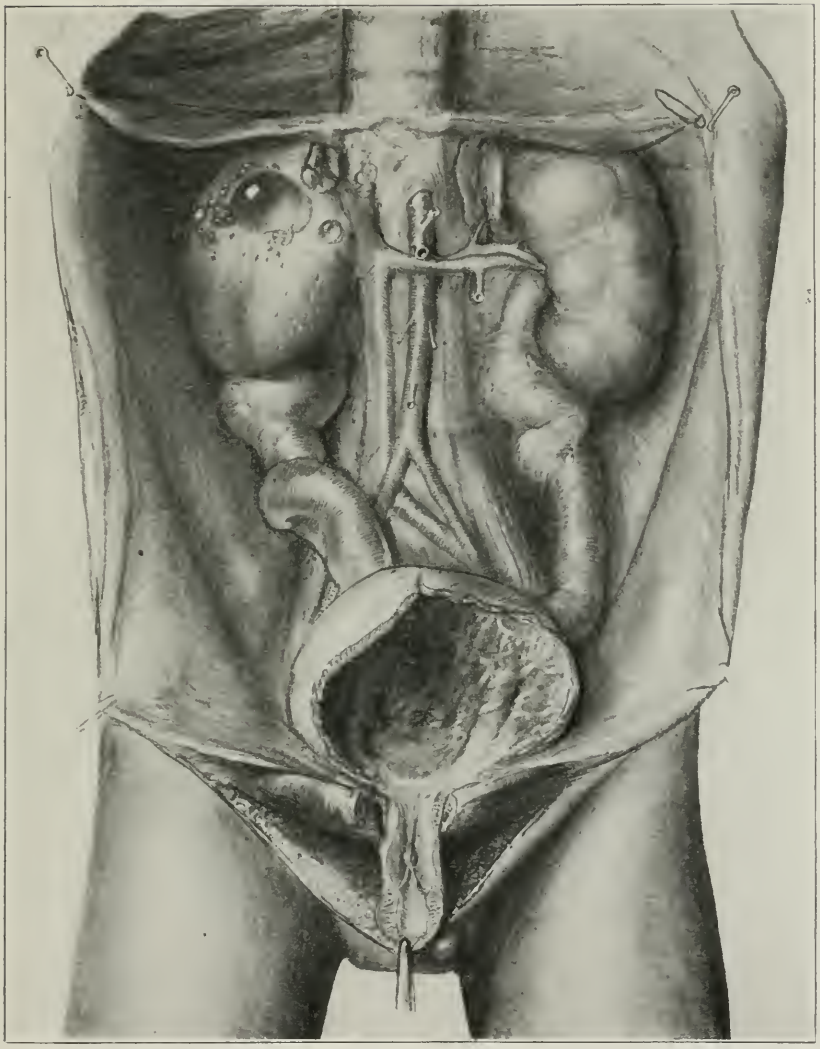

Fig. 1.—Drawing at autopsy by J. P. Webster. Note the enlarged, lobulated cystic kidneys, the enormously dilated and tortuous ureters; the hypertrophied, distended bladder and the hypertrophied membranous folds in the prostatic urethra constituting the obstruction to the urinary flow.

MICROSCOPIC DESCRIPTION

Urethra: Sections were prepared from the lower end of the prostatic sac; through the folds immediately below the verumontanum; through the distal portion of the verumontanum; and through the proximal end of the same structure. The blind end of the prostatic urethra is clothed with stratified pavement epithelium similar to that of the esophagus. The folds below the verumontanum are covered with the same type of epithelium but that of the anterior urethra is so badly desquamated that its nature cannot be definitely determined. Over the verumontanum and the rest of the prostatic urethra, the usual type of epithelium is present. The subepithelial tissues everywhere consist of a very dense, fibrous tissue with few elastic elements. Small clusters of mononuclear cells may be found occasionally beneath the epithelium. The vagina masculina is not prominent. Indeed, it is less conspicuous than is often the case.

Bladder: The bladder wall is thick, the muscle bundles large. The mucosa shows scattered mononuclear cells. The epithelium of the mucosa is not preserved.

Ureter: The ureter, also, is greatly thickened and contains many elastic fibers. The epithelium is of the normal type and very well preserved.

Kidney (Fig. 2): Examination under a dissecting lens reveals the whole width of kidney parenchyma much narrowed. The medullary portion is no longer pyramidal in shape but is flattened out, the tubules running almost parallel with the lining of the dilated calyces. The tubules of the cortex are enormously enlarged being quite prominent even under the power of the dissecting microscope. With higher power the epithelium of the pelvis is found well preserved. Beneath it the mucosa is infiltrated with plasma cells and contains no elastic elements. The connective tissue between the straight tubules in the medulla is thickened and contains scattered mononuclear cells. The walls of the larger blood-vessels are thickened. This is especially true of the intima. The capsule of the kidney is considerably thickened and extending down from it in places may be seen strands of connective tissue. Between these connective tissue strands the tubules are markedly hypertrophied with wide lumina and very large cubical or flattened granular cells, whose nuclei stain well. The lumen of each tubule contains a foamy material and occasionally a hyaline cast. The glomeruli are few in number, but those present seem very nearly normal. Here and there one which is imbedded in a connective tissue strand is entirely hyaline or shows some hyaline change.

Sections from other organs show nothing of interest in this connection, save, perhaps, those from the right adrenal. The tumor-like nodules consist of large nests of epithelial cells separated by connective tissue trabeculae, some of which are extensively calcified. The appearance and arrangement of the cells is strongly suggestive of the normal adrenal cortex. The cells, however, contain practically no fat or lipoid substances.

SUMMARY OF CASE

In summary, we present the case of a boy 5 years old, who had had difficulty in controlling micturition from infancy. Urine passed every half hour of day and night, and was attended by no pain.

Four weeks before death there occurred a sudden onset of the terminal illness with cough, abdominal pain, vomiting and constipation. Physical examination showed malnutrition, purulent conjunctivitis, discharge from left ear, tonsillar abscess, protuberant abdomen, a tumor above the

symphysis, with dull percussion note, redundant foreskin with phimosis: hemoglobin 70 per cent. There was no fever. Later vomiting became frequent, there were many convulsive attacks and breathing suggestive of air hunger. He was circumcised three weeks before death with the result of slightly improving the flow of urine. Attempt at catheterization failed.

At autopsy there was found an obstruction in the prostatic portion of the urethra, which was converted into a blind pouch by the fusion

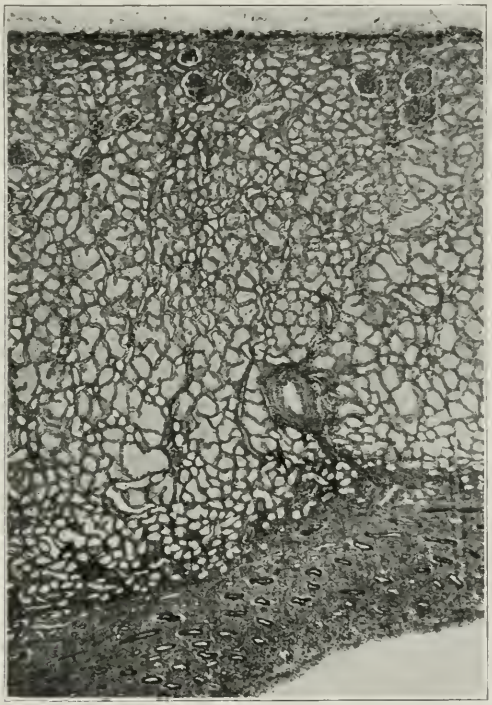

Fig. 2.—Section of kidney under low power. The glomeruli appear normal; tubules of cortex are greatly dilated; tubules of medullary portion are compressed and run parallel to lining of dilated calyces.

of its anterior and posterior walls, due apparently to an overdevelopment of folds normally present immediately distal to the verumontanum. A small triangular opening whose sides measured 3 mm. situated in the floor of this pouch was the only communication with the anterior urethra and through this the urine must pass. As a result of the urinary stasis

there had occurred marked dilatation and hypertrophy of bladder, ureters and kidney pelves with typical hydronephrosis terminating in uremia.

Aside from the condition in the urethra, no other congenital anomaly was discovered unless the adrenal adenoma may be so considered.

INCIDENCE OF CONGENITAL URETHRAL OBSTRUCTION

While the condition here described and other types of congenital urethral obstruction cannot be considered of frequent occurrence, neither are they excessively rare and we feel, after reviewing the literature, that they may be met with more frequently than is generally supposed.

Very similar cases, some of them almost identical with ours, are reported by Wilckens,[1] Lederer,[2] Tolmatschew,[3] Bednar,[4] Godart,[5] Budd,[6] Velpeau,[7] Schlagenhaufer,[8] Commandeur,[9] Bonnet,[10] Reboul,[11] Fuchs,[12] Porak,[13] Lindeman,[14] Picard.[15] In addition Bazy[16] reports six cases, in older boys and in men, which he had observed clinically, as cases of congenital stricture in the region of the pars membranacea or pars bulbosa and emphasizes the importance of congenital strictures of the urethra

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1. Wilckens: Zur Frage der kongenitalen Stenosen der männlichen Harnröhre. Ztschr. f. Urol., 1910, iv, 814.

2. Lederer: Ueber eine angeborene membranöse Verengerung der Pars prostatica urethrae. Arch. f. path. Anat. u. Physiol., Berl., 1911, cciii, 240.

3. Tolmatschew: Ein Fall von semilunaren Klappen der männlichen Harnröhre und von vergrösserter Vesicula prostatica. Arch. f. path. Anat. u. Physiol. Berl., 1870, xlix, 348.

4. Bednar: Quoted from Wilckens,[1] Lindeman[14] et al.

5. Godart: Valvule anormale dans le canal l'urètre. Bull. Soc. anat. de Paris, 1854, xxix, 137.

6. Budd: Quoted from Wilckens,[1] Lindeman[14] et al.

7. Velpeau: Traité d'anatomie chirurgicale, Paris, 1826, ii, 297.

8. Schlangenhaufer: Ein Beitrag zu den angeborenen Klappenbildungen im Bereiche der Pars prostatica urethrae. Wien. klin. Wchnschr., 1896, No. 15, p. 268.

9. Commandeur: Dilatation de l'appareil urinaire chez le foetus par rétrécissement valvulaire congénital de l'urètre. Lyon méd., 1898 Mars. 13.

10. Bonnet: Quoted from Wilckens.[1]

11. Reboul: Quoted from Wilckens.[1]

12. Fuchs: Zwei Fälle von kongenitaler Hydronephrose. Inaug. Dis., Zurich, 1900.

13. Porak: Quoted from Commandeur and Lederer.[9]

14. Lindeman: Casuistischer Beitrag zur Frage der angeborenen klappenförmigen Verengerung der Pars prostatica urethrae. Inaug. Dis., Jena., 1904.

15. Picard: Convulsions à forme eclamptique chez un homme, Gaz. méd. de Strassburg, 1855, No. 7, p. 259. Quoted from Lindeman.[14]

16. Bazy: Rétrécissement congénital de l'urètre chez l'homme. Presse méd., 1903, p. 215.

even in adults. Ebert[17] reports a similar clinical case in which he punctured the obstructing membrane and discharged his patient as cured. There are numerous other reports of congenital stricture in the anterior urethra, due to valve-like structures, partial or total occlusion of the urethra throughout a smaller or greater portion of its extent, atresia of the external meatus, etc. Englisch,[18] in a recent exhaustive article, has collected a large number of cases of congenital narrowing of the male urethra.

Most of the published observations similar to the case here recorded occurred in new-born children, or babies a few days or weeks old. A number, however, have been observed in older children, in whom the lesions seem to have remained latent for a time and then gradually became more severe. Budd's patient was 16 years old, Lederer's 11, Wilckens' 2¼, our one case 5. Picard regarded the valve-like lesion in his 40-years-old patient as of congenital origin. The symptoms are dated in three of these cases from an attack of one of the acute infections.

SYMPTOMATOLOGY

Of the instances observed in older children, the case here reported is quite typical if we accept those symptoms due to the local infections in the middle ear, tonsils, etc. In the new-born infants and babies a few days old the symptoms are of course simpler and consist in the extreme cases of failure to pass any urine whatever.

PATHOLOGY

Englisch[19] divides all congenital obstructions in the urinary passages of children into two great groups:

A. Obstructions which exist in embryonic life, but later disappear.

B. Obstructions which remain permanently.

Under Group "A" he includes the fusion of epithelial folds in the ureters; a similarly produced atresia of the ureteral opening into the bladder: valve formation and kinkings of the ureters which disappear with subsequent growth: atresia of the internal or of the external meatus of the urethra: atresia of the prepuce: and finally atresia of the orifices of the utriculus masculinus and of Cowper's glands.

17. Ebert: Quoted from Segall. Ein Fall von angeborener Harnröhrenverengerung. Inaug. Dis., Königsberg. 1890.

18. Englisch: Ueber angeborene Verengerungen der männlichen Harnröhre. Folia urologica. 1909. iv and v.

19. Englisch: Quoted from Wilckens.[1]

Under Group "B" are found the valves and stenoses. The valves occur at the transition between ureters and kidney pelvis, rarely in the bladder; especially in the prostatic part of the urethra at the upper and lower ends of the colliculus seminalis; in the anterior urethra at the end of the fossa navicularis, at the external meatus and even in the foreskin.

The places of predilection of the stenoses in the urethra are especially the point of union of the pars membranacea with the pars bulbosa, the posterior end of the fossa navicularis and the external urethral orifice.

The folds or valve-like obstructions in which we have been most interested seem to occur in those regions where folds or ridges are normally found in the urethral mucosa; and this is especially true of the anterior end of the colliculus seminalis where most of these obstructions are encountered. Here in the normal urethra there is a division of the crista urethralis into two ridges which, becoming less and less prominent, gradually fade out in the posterior wall of the bulbous urethra.

In most of the reported cases of obstruction at this point, the lesion seems to have been produced by an overdevelopment of these folds which fuse with the anterior wall with the formation of membranes extending across the urethral lumen. The resulting structures vary slightly in individual cases. Schlagenhaufer describes the obstruction in his case as due to a funnel-shaped valvular occlusion. In others the pressure of the urine has resulted in a more definite pouch, with this concavity of the membranes directed backward toward the bladder. The size and relationships of the opening through the obstruction vary also, and this is of considerable practical importance in the clinical examination. A sound introduced into the urethra may pass quite unhindered into the bladder, as in the case reported by Bednar, or the opening may be so small and so situated immediately below an enlarged verumontanum, as in our own case, that the smallest catheter is obstructed.

Budd, Godart and others compare the obstructing membrane to the valves of a vein or to the semilunar valves of the heart. In these cases no interference is offered to the passage of an instrument from below.

The secondary pathologic changes are quite uniform in kind, differing only to a certain extent in degree. There is invariably dilatation and hypertrophy of the higher urinary passages with bilateral hydronephrosis.

Histologic examination shows a metaplasia of the epithelium in the posterior urethra from the usual transitional type to a stratified squamous type like that of the epidermis.

GENESIS

The occurrence in young children and the similarity of the pathologic anatomic pictures in different cases establish the lesion as congenital and suggest strongly that it has its origin in some slight variation from the normal in the course of development. It must then be through study of the embryology of this region that we shall finally arrive at a satisfactory explanation for these anomalies. At present this is not to be found.

Certain forms of obstruction in the prostatic urethra have a ready explanation in the present state of our knowledge of embryology. Those due to the abnormal persistence of Müller's ducts in the male come under this class. In an over-development of the sacculus prostaticus, the homologue of the vagina, this structure may become so large that it is pushed out into the urethra and may block the flow of urine. The outer genitalia may show no abnormality.

Again, in analogy to the "hymen imperforatus" in women, the sacculus prostaticus, utericulus prostaticus, or vagina masculina, as it is variously named, may be closed at its urethral end. This may be associated with a cystic widening of the utricle which leads to urine retention. Such lesions are attributable to more or less slight degrees of pseudohermaphrodism.

Concerning the development of the folds in the mucosa constituting the crista urethræ, we have been able to find little or nothing. We do not know what the relationship is, if indeed there is any, between these folds and the prostatic utricle, the remains of Müller's ducts. They are said to bear some relationship to the developing prostate gland.[20]

Two principle views are presented in the literature by students of these cases. One of these is that the abnormality is due to an over-development of folds normally present in the mucosa, and no explanation is attempted of the initial stimulus to growth. Englisch is of the opinion that after the establishment of a certain grade of obstruction, the pressure of the urine exerts a continuous irritation on this region with the stimulation of epithelial growth and production of proliferative inflammatory changes which account for the gradual increase in the efficiency of the obstruction and in the gravity of the symptoms.

Posner,[21] Wilckens and especially Lederer are inclined to regard this lesion as a malformation due to arrested development. Lederer says in

20. Lowsley: Personal communication (Article in press). Am. Jour. Anat., June 15, 1912.

21. Posner: Ueber angeborene Strieturen der Harnröhre. Berl. klin. Wchnschr., 1907, xliv, 275.

favor of this view that it occurs at about the point of union between the entodermal and ectodermal portions of the urethra.

Recent workers in human embryology are at variance in their views on the development of the urethral canal. Felix,[22] who writes the exhaustive article on the development of the urinary and sexual organs in Keibel and Mall's system of Human Embryology, insists that the whole canal from the verumontanum to the sulcus coronarius glandis is developed from the sinus urogenitalis and is of entodermal origin. Broman,[23] on the other hand, in his recent work accepts the view that the corpus cavernosa urethræ is developed from the ectodermal or cloacal plate. Certainly this latter view would furnish the better explanation for the numerous anomalies occurring in the membranous and anterior portions of the urethra, including, perhaps, such valve-like structures as those described by Posner at the junction of the pars membranacea and the pars bulbosa. But even should we adhere to this view, the lesion we have described in the posterior urethra, is too far posterior to be ascribed to a failure in the union of entodermal and ectodermal structures. In the lack of definite knowledge we lean rather to the view that we are dealing with a simple progressive malformation and not one due to arrest of development. Certainly, the region in which this anomaly occurs is one of complex development, being the point of union of the prostatic urethra developing from the mesodermal wolffian ducts, the urethra distal to the verumontanum derived from the entodermal-sinus urogenitalis, the prostatic utricle representing the remnants of Müller's ducts and the ejaculatory ducts.

CONCLUSIONS

We have been able to find no case of congenital membranous obstruction occurring in the prostatic urethra reported in full in our American literature and yet the condition has not been infrequently described abroad.

We believe that the possibility of interference with the urinary flow from such a congenital malformation should be considered whenever the cause of the obstruction is not obvious; especially should there be a persistently distended bladder. A partial obstruction of this nature is

22. Felix: Die Entwicklung der Harn- und Geschlechtsorgane. Handbuch der Entwicklungsgeschichte des Menschen. (F. Keibel and F. P. Mall), ii, 732.

23. Broman: Normale und abnorme Entwicklung des Menschen. Wiesbaden, 1911 (J. F. Bergmann), p. 476.

compatible with the passage of a normal daily amount of urine, but there may be either increased frequency of micturition or incontinence if the lumen is not absolutely occluded.

The condition if recognized in most instances could be easily corrected.

Autopsy findings should not be considered complete without incision through the anterior urethral wall and inspection of the complicated structures in or near the pars prostaticus.

We wish to thank Dr. Llewellys F. Barker for the privilege of reporting the case from his wards, and Mr. J. P. Webster for the excellent drawing.

DISCUSSION

DR. GRIFFITH said that he had in his possession photographs of a case occurring in the practice of a colleague in the dispensary of the Children's Hospital, which showed a condition analagous in some respects to that described. The infant soon after birth developed great distention of the abdomen, which was found later to depend on an unusually distended bladder, the urine being unable to find exit.

STUDIES IN METABOLISM OF AMAUROTIC FAMILY IDIOCY

HENRY HEIMAN, M.D., SAMUEL BOOKMAN, PH.D., AND BURRILL B. CROHN, M.D.

NEW YORK

PART I.—BY HENRY HEIMAN, M.D.

Carefully as this disease has been observed for over a quarter of a century, the obscurity regarding its true nature is still as great as ever. While Sachs'[1] somewhat modified view of its congenital origin has gained many adherents, among these such careful observers as Schaeffer[2] and Vogt,[3] there are a considerable number of authorities who hold the opinion that this affection is acquired in nature. Though few now share the view of Hirsch[4] that some toxic substance plays a rôle in the etiology of the disease, it is on theoretical grounds alone that it has been discarded. Yet this view is not so wholly improbable or unreasonable as not to demand better founded reasons for its final abandonment. Moreover, within recent years certain observations have been recorded which seem to indicate that other organs besides the nervous system are affected in this disease. Thus Brooks[5] has found morbid changes in the pancreas, hypophysis, thymus and adrenals. If toxic agents are at work, and more especially if the organs playing an important rôle in the production of internal secretions are affected, we may expect that the metabolic processes would show some departure from the normal.

In view of the fact that this disease is so prominently characterized by a marked and generalized degeneration of nerve cells and nerve tissue, as proved by the very thorough recent histologic and pathologic studies of Schaffer, Vogt, Brooks, Sachs and Strauss,[6] and others, it would be interesting to discover in the excretions the chemical evidences of the

1. Sachs: Jour. Nerv. and Ment. Dis., 1887.
2. Schaffer: Jahrb. f. Psychol. u. Neurol., 1907, p. 121; Ztschr. d. Jugend. Schwach., No. 2, p. 75; *ibid* No. 3, p. 19.
3. Vogt: Archiv. f. Kinderh., 1909, li.
4. Hirsch: Jour. Nerv. and Ment. Dis., 1898, p. 538.
5. Brooks: Tr. Assn. Am. Phys., 1911.
6. Sachs and Strauss: Jour. Exper. Med., 1910, xii, 685.

degenerative process which we know is going on. This should be evidenced by some disturbance in the excretion of those elements which are so integral a part of nerve tissue, namely, phosphorus and sulphur. Despite the valuable information that could be expected from a chemical study, this aspect of the disease has been, up to the present, almost entirely neglected. A perusal of the recent literature fails to show any extended metabolic studies. The only investigation dealing with the chemical side of amaurotic family idiocy is that of Mott. In a paper detailing the chemical analysis of the brain in two cases of amaurotic family idiocy, Mott[7] shows a very distinct change in the relative proportions of simple and nucleoproteins, the latter being diminished, and being replaced by proteins of a simpler composition with an increased water content.

The opportunity having presented itself of observing two cases of this disease, it seemed worth while to undertake the study of its metabolism. As will be seen from the hospital records, both were typical cases of amaurotic family idiocy. The first case was submitted to one period of investigation, the second to two at an interval of twenty-four days.

CASE REPORTS

Case 1.—The first case, David F., 15 months old, born in the United States, of Russian Jewish parentage, was admitted to the children's service of Dr. Koplik at the Mount Sinai Hospital, April 7, 1911. One other child was well.

Past History.—Full term, breast-fed for twelve months; enterocolitis of two months' duration at 6 months of age; measles at 12 months of age; never sat up nor stood up, nor made any attempt to speak; no history of convulsions. Since the attack of measles three months prior to this report, mother noted gradually increasing drowsiness and weakness. There was no vomiting, no fever, no other disturbances, but marked sweating especially at night. Bowels markedly constipated.

Physical Examination.—General condition fair, well nourished; no rigidity of neck; eyes staring, apparently blind; right pupil larger than left; pupils react sluggishly; heart, lungs, and abdomen negative; spasticity of all four extremities; reflexes not obtained.

April 28, 1911. Fundi show cherry-red colored spot in the center of a white area outside of each disk, which is atrophic and white.

Urine negative.

During the stay in the hospital, the condition of the patient did not change.

Case 2.—The second case, H. Sch., aged 7 months, born in the United States, of Russian Jewish parentage, was admitted to the hospital Sept. 12, 1911. Family history negative. Four other children well; no miscarriages.

Past History.—Breast-fed up to time of examination. At 14 weeks of age the child had an attack of bronchitis for nine days. Mother dates illness from that time. No other diseases.

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7. Mott: Arch. Neurol., Path. Lab., London County Asylum, iii, 218.

Present History.—Since attack three months prior to this report, the mother had noticed that child no longer played, but slept most of the time. Does not take the breast as readily, does not sit up, and can not stand. Child apparently can not hear or see as well as it should. No convulsions; no vomiting. Bowels move twice daily.

Physical Examination.—General condition good; patient well nourished; slightly anemic. Internal strabismus; eyes apparently follow light. Hearing normal. Loud blowing systolic at apex, heard with greatest intensity in third and fourth interspaces. Lungs negative. Liver palpable two fingers below rib border. Spleen negative. Spasticity of both upper and lower extremities; knee-jerks normal; no ankle clonus. Cherry-red spot present. Noguchi test negative. Urine negative.

Most important in a consideration of the metabolism of such a condition as amaurotic family idiocy is the stage of the disease and the general condition of nutrition of the patient under investigation. The two children studied by us were both in an early period of this insidious malady; their general nutrition was good, muscular tissue still very well preserved, and an abundant panniculus adiposis present. So good was the general health of the children, that during the periods of observation in both cases a gain of weight was noted. Thus the patient, David F., gained 180 gm.; Patient 1, H. Sch., gained in the four days of the first investigation 80 gm.; in the second period, 30 gm. In all these instances the nourishment was well taken, the diet consisting of milk undiluted in Case 1, and diluted in Case 2. The caloric intake was in excess of the established figures of Heubner (100 calories per kilo per day).

TABLE 1.—INVESTIGATION DURING A FOUR-DAYS PERIOD OF THE DAILY NOURISHMENT OF DAVID F. (CASE 1), AGED 15 MONTHS

	Ounces	Calories
Milk	27	560
Cocoa	9	200
Broth	5	10
		770

Weight 8.4 kilos equals 95 calories per kilo per day.

TABLE 2.—DAILY NOURISHMENT OF SCH. (CASE 2), AGED 7 MONTHS

	Ounces	Calories
Milk	36	730
Maltose	1½	180
		910

Weight 7.65 kilos equals 119.3 calories per kilo per day.

The minute details of this metabolic study will be given in the second part of this paper by Drs. Bookman and Crohn. The general results of the present investigation are shown in the accompanying tables:

TABLE 3.—METABOLISM STUDY; INTAKE, OUTPUT AND DAILY AVERAGES IN AUTHORS' CASES

	N	S	P	Cl
INTAKE				
David F.	5.831	0.5087	0.6997	1.529
Sch. (I)	3.220	0.521	0.393	0.753
Sch. (II)	5.610	1.084	1.115	1.253
URINE				
David F.	2.834	0.23235	0.3553	0.581
Sch. (I)	1.2382	0.1075	0.121	0.3115
Sch. (II)	3.078	0.302	0.255	0.862
STOOL				
David F.	0.225	0.0775	0.0496	.....
Sch. (I)	0.2385	0.0424	0.0104	.....
Sch. (II)	0.076	0.084	0.1924	.....
TOTAL OUTPUT				
David F.	3.059	0.3099	0.4040	0.581
Sch. (I)	1.4767	0.1499	0.1313	0.3115
Sch. (II)	3.154	0.388	0.4482	0.862

TABLE 4.—METABOLISM STUDY IN AUTHORS' CASES. DAILY AVERAGES

	N	N %	S	S %	P	P %	Cl	Cl %
RETENTION (PER CENT. OF INTAKE)								
David F.	2.772	47.5	0.1989	39.1	0.2951	42.2	0.948	62.0
Sch. (I)	1.744	54.15	0.371	71.2	0.262	66.6	0.441	58.6
Sch. (II)	2.456	43.9	0.6985	64.4	0.6665	60.0	0.391	31.0
ABSORPTION (PER CENT. OF INTAKE)								
David F.	5.6055	96.0	0.431	84.8	0.6505	93.0	.....	....
Sch. (I)	2.9815	92.5	0.4786	91.7	0.3826	97.6	.....	....
Sch. (II)	5.534	98.6	1.000	92.2	0.9222	82.8	.....	....

From a perusal of the data before us, we are struck by the fact that absorption from the gastro-intestinal tract and retention within the body are normal, or even better than normal, for all the constituents determined. Thus, David F. absorbed 97 per cent. of nitrogen, the normal being 88 to 96 per cent.; retention 50 per cent., the normal being 30 per cent. at this age.

Close scrutiny of the figures for the intake and output of phosphorus and sulphur does not disclose a marked disturbance in the metabolism of these constituents. As has been before stated, absorption and retention are unusually good and increased beyond normal, probably indicating a hypernormal anabolic function occurring at this stage of the disease. However, when one takes into consideration the very slow process of degeneration, extending over a period of months or years, and the very

small amount of actual phosphorus and sulphur in the entire cerebrospinal system, one can understand why, with our present methods, an abnormal elimination of these constituents would fail to be manifested in a study of this disease for short periods. It would be advisable, therefore, to study the disease at intervals during its course, both in its earlier stages in which anabolic changes apparently predominate, and in its later stages in which degenerative and catabolic processes play the important rôle.

PART II.—BY SAMUEL BOOKMAN, PH.D., AND BURRILL B. CROHN, M.D.[8]

This rather rare disease, first identified and studied by Tay and Sachs, has been subjected during the last few years to most searching investigations in regard to its clinical, pathological and histological aspects. The numerous publications throughout the literature are most complete along these lines; we fail, however, to find any work dealing with the closer examination of the metabolic changes, if any, which accompany the morbid processes which characterize the malady in question. It occurred to us, therefore, to investigate whether the very marked pathological changes which have been repeatedly demonstrated, viz., the universal and generalized degeneration of the neurons, involving all the nerve cells, including the ganglion cells, both central and sympathetic, might not find its concomitant in some abnormal chemical variations.

With this end in view, two cases, D. F. and H. Sch., were subjected to complete metabolism studies. In each instance the patient was put onto a Heubner metabolism bed for four days. The diet was made up into exact duplicates, one of which was fed to the child, the second utilized for analysis. Urine and stool were separated by collecting the stool on a sieve, the urine being allowed to percolate through into another receptacle, and estimated every six hours, being then put on ice to prevent decomposition. The whole stool was collected for each period, sampled and analyzed. The analytical methods employed were as follows:

8. From the Laboratory of Physiological Chemistry, Pathological Department, Mt. Sinai Hospital.

The cases on which this study is based, were assigned from the service of Dr. Henry Koplik, attending physician, and Dr. Henry Heiman, associate attending physician to the children's service of Mt. Sinai Hospital. We wish to express our thanks to Drs. Koplik and Heiman for kind cooperation throughout the work in the wards; also to Dr. Theodore Kuttner for valuable assistance in chemical analyses.

ANALYTICAL METHODS

Total nitrogen, Kjeldahl method.

Total phosphorus and total sulphur by fusion with sodium hydrate and nitrate.

Chlorin, incineration with sodium, carbonate and nitrate, and titration with silver nitrate. In the urine preformed sulphates in acetic acid solution, and barium chlorid, ethereal sulphate in the filtrate by further boiling with hydrochloric acid.

Total sulphates were determined by direct precipitation in hydrochloric acid solution by barium chlorid.

Neutral sulphur was estimated by difference between total sulphur and total sulphates.

Total phosphates in the urine by titration with uranium acetate (Neubauer's method).

Ammonia by the Folin aeration method.

Total acidity of the urine by titration with N/10 ammonium hydrate, using phenolphthalein as an indicator.

The stool was dried in the water-bath, after addition of alcohol and hydrochloric acid (chlorin in stool not estimated).

CASE 1.—D. F., male, aged 15 months. One period of four days. Weight at beginning of period 8.12 kg.; weight at end of period, 8.3 kg.; diet, 48 ounces of whole milk per day; calories, 120 per kilogram. Slight but negligible vomiting occurred. (See Table 5.)

CASE 2.—(Sch.) This patient was subjected to two studies of four days each, with an interval of three weeks between the two periods.

Period I. Age 7½ months; weight at beginning of period, 7.39 kg.; weight at end of period, 7.47 kg.; diet 121 calories per kilogram. (See Table 1.)

Period II. Age 8¼ months; weight at beginning of period, 7.53 kg.; weight at end of period, 7.56 kg. (See Table 6.)

TABLE 5.—METABOLISM EXPERIMENT IN CASE 1

D. F., period four days; age 15 months; weight 8.125 kg. Nourishment equals 48 ounces of whole milk (raw), equals 975 calories per day or 120 calories per kg. of weight.

INTAKE

Date	N	S	P	Cl
5/3	5.323	0.5447	0.8076	1.4306
5/4	7.302	0.4819	0.7890	1.3470
5/5	4.998	0.4406	0.5024	1.5590
5/6	5.702	0.5676	0.6997	1.7790
Total	23.3250	2.0348	2.7987	6.1156
Daily average	5.831	0.5087	0.6997	1.5290

OUTPUT—URINE

Date	Amount c.c.	Acidity	NH_3	N
5/3	490	123.9	0.1647	2.894
5/4	480	104.8	0.4000	2.432
5/6	480	100.8	0.0618	2.842
5/6	560	alk.	.....	3.167
Total	...	.....	.....	11.335
Daily average	...	.....	.....	2.834

OUTPUT—URINE

Date	Sulphur: Preformed SO_3	Sulphur: Ethereal SO_3	Sulphur: Totals	P_2O_5 as P	Cl
5/3	0.1810	0.00578	0.2295	0.3004	0.653
5/4	0.1664	0.00817	0.1969	0.3379	0.511
5/5	0.2086	0.01262	0.2398	0.3845	0.579
5/6	0.2371	0.00239	0.2632	0.3986	0.581
Total	0.7931	0.05047	0.9294	1.4214	2.324
Daily average	0.1983	0.01262	0.23235	0.35535	0.581

STOOL

	N	S	P
For period	0.902	0.30996	0.1969
Daily average	0.2254	0.07749	0.04922

TABLE 6.—METABOLISM EXPERIMENTS. DAILY SHEET. CASE 2

Sch., aged 7½ months; weight 7.39 kg.; nourishment, per day:

	gm. or c.c
Whole (raw) milk	960
Water	360
Maltose	45

Caloric value=910 calories or 121 calories per kg. weight.

PERIOD I—INTAKE

Date	N	S	P	Cl
9/19	3.3200	0.3964	0.3933	0.4700
9/20	2.8710	0.4317	0.2758	0.6700
9/31	2.4100	0.4290	0.3124	0.6600
9/22	4.2810	0.8252	0.5918	1.2100
Total	12.8820	2.0823	1.5733	3.0100
Daily average	3.2200	0.5201	0.3930	0.7530

OUTPUT—URINE

Date	Amt. c.c.	Acidity	NH_3	N	S	P_2O_5 as P	Cl
9/19	325	143	0.273	1.2376	0.1104	0.1499	0.4499
9/20	250	102.5	0.292	1.4560	0.1047	0.1357	0.2573
9/21	215	alk.	.....	1.0234	0.1000	0.1017	0.1526
9/22	320	alk.	.....	1.2360	0.11498	0.0966	0.3860
Total	...	.....	.....	4.9530	0.4301	0.4839	1.2458
Daily average	...	.....	.....	1.2382	0.1075	0.1210	0.3115

STOOL

	N	S	P
For period 9/19 to 9/22, 29.5 gm.	0.954	0.1697	0.0413
Daily average	0.2385	0.0424	0.0104

TABLE 7.—METABOLISM EXPERIMENT. CASE 2

PERIOD II—INTAKE

Date	N	S	P	Cl
10/13	5.61	0.915	0.936	0.937
10/14	5.34	1.092	0.896	1.312
10/15	5.984	1.191	1.493	1.461
10/16	5.505	1.139	1.144	1.303
Total	22.439	4.337	4.459	5.013
Daily average	5.610	1.084	1.115	1.253

OUTPUT—URINE

Date	Amt. c.c.	Acidity	NH_3	N	S	P_2O_5 as P	Cl
10/13	730	73	0.3808	3.026	0.3927	0.1495	0.855
10/14	780	alk.	.....	3.177	0.2986	0.3192	0.886
10/15	750	alk.	.....	3.297	0.2133	0.2445	0.958
10/16	660	alk.	.....	2.810	0.3025	0.3086	0.749
Total	...	...	.....	12.310	1.2071	1.0218	3,448
Daily average	...	...	.....	3.078	0.3020	0.2555	0.862

STOOL

	N	S	P
For period 10/13 to 10/16	0.305	0.336	0.771
Daily average	0.076	0.084	0.1928

For a more comprehensive comparison of the above tables, we have seen fit to rearrange these in terms of daily average figures (Table 8).

TABLE 8.—INTAKE AND OUTPUT—DAILY AVERAGES

	N	S	P	Cl
INTAKE				
Sch. I	3.220	0.521	0.393	0.753
Sch. II	5.610	1.084	1.115	1.253
D. F.	5.8310	0.5087	0.6997	1.529
URINE				
Sch. I	1.2382	0.1075	0.121	0.2115
Sch. II	3.078	0.302	0.255	0.862
D. F.	2.834	0.23235	0.3553	0.581
STOOL				
Sch. I	0.2385	0.0424	0.0104	.....
Sch. II	0.076	0.084	0.1924	.....
D. F.	0.225	0.0775	0.0496	.....
TOTAL OUTPUT				
Sch. I	1.4767	0.1499	0.1313	0.3115
Sch. II	3.154	0.388	0.4482	0.862
D. F.	3.059	0.3099	0.4040	0.581

Further, more carefully to analyze the individual factors entering into this metabolism study, we offer the tables and the conclusions derived therefrom (Table 9).

TABLE 9.—NITROGEN METABOLISM. DAILY AVERAGE

	Intake	Urine	Stool	Absorption	Absorption, Per cent.	Retention	Per cent. of Intake
Sch. I	3.220	1.2382	0.2385	2.9815	92.5	1.744	54.15
Sch. II	5.610	3.078	0.076	5.534	98.6	2.456	43.9
D. F.	5.831	2.834	0.2254	5.6055	96.0	2.772	47.5

NITROGEN METABOLISM

Case 2 (Sch.) may be compared to the results of Rubner and Heubner[9] in the study of a normal child of the same age. The retention of nitrogen in our case is markedly increased. The absorption is slightly higher in our case than in the one of Rubner and Heubner, although not exceeding normal variations (Table 10).

TABLE 10.—FIGURES FOR NITROGEN METABOLISM OF NORMAL CHILDREN (FROM SEVERAL AUTHORS) APPROXIMATELY SAME AGE AND WEIGHT AS CASE 2

	Intake	Urine	Stool	Absorption	Per cent.	Retention	Per cent.
Rubner and Heubner,[9] child 7½ months	4.26	3.067	0.281	3.979	93.4	0.912	36.7
Klotz,[17] child 6 months	6.863	4.2625	0.8402	6.0231	87.7	1.76	25.6

Case 1 may be compared to Child B of Camerer[10] of approximately the same age and in good health. The retention of nitrogen in our Case 2 on an intake of 5.8 gm. was 47.5 per cent., absorption 96 per cent. In Camerer's case, however, the retention was only 6 per cent. In both of our cases, therefore, absorption and retention are considerably increased. By comparison with Cronheim and Meyer's[11] figures, these deductions are further substantiated (Table 11).

TABLE 11.—FIGURES FOR NITROGEN METABOLISM OF NORMAL CHILDREN (FROM SEVERAL AUTHORS) APPROXIMATELY SAME AGE AND WEIGHT AS CASE 1

	Intake	Urine	Stool	Absorption	Per cent.	Retention	Per cent.
Camerer,[10] child 1 year	5.0	4.0	0.7	4.3	86	0.3	6.0
Cronheim and Meyer,[11] child 6 6 months	4.454	3.182	0.530	3.923	89	0.741	16.7
Cronheim and Meyer, child 6 months	4.454	3.057	0.452	4.001	90	0.945	21.3

CHLORIN METABOLISM

In the absence of figures for normal children of this age on similar diet, it is impossible to do more than note the high chlorin retention in

9. Rubner and Heubner: Ztschr. f. Biol., 1899, No. 38, p. 315.
17. Klotz: Jahrb. f. Kinderh., 1909, No. 70, p. 1.
10. Camerer: Stoffwechsel des Kindes.
11. Cronheim and Meyer: Biochem. Ztschr., 1908, ix, 80; Ztschr. f. Biol., No. 27, p. 153.

our cases (Table 12). L. F. Meyer[12] averages several previously published analyses of healthy children on mother's milk and shows but 42 per cent. retained chlorin on an intake of only 20 to 40 per cent. of that of our cases. This emphasizes the fact that the retention in our cases of 31 per cent. to 62 per cent. is remarkably high (Table 13).

TABLE 12.—CHLORIN METABOLISM. DAILY AVERAGE

	Intake	Urine	Stool	Retention	Per cent.
Sch. I	0.753	0.3115	*	0.441	58.6
Sch. II	1.253	0.862	...	0.391	31
D. F.	1.529	0.581	...	0.948	62

*As HCl was added to stool in the drying process, no Cl estimations were possible.

TABLE 13.—CHLORIN METABOLISM IN HEALTHY CHILDREN (MOTHER'S MILK DIET)

	Intake	Urine	Stool	Absorption	Per cent.	Retention	Per cent.
L. F. Meyer ..	0.3217	0.1776	0.0135	0.3162	96	0.1386	42

PHOSPHORUS METABOLISM

The phosphorus metabolism also is noticeable for its high retention as evidenced by the figures in Table 14. Unfortunately, Keller's[13] figures in an article devoted to studies on phosphorus metabolism are not strictly comparable, for the reason that the children he studied were suffering from gastro-intestinal disturbances; neither was the intake noted, nor the excretion of phosphorus in the stool estimated.

TABLE 14.—PHOSPHORUS METABOLISM. DAILY AVERAGE

	Intake	Urine	Stool	Absorption	Per cent.	Retention	Per cent.
Sch. I as P	0.3930	0.1210	0.0104	0.3826	97.6	0.262	66.6
as P_2O_5	0.9039	0.2783	0.0239	.....	....	....	....
Sch. II as P	1.115	0.25545	0.1928	0.9222	82.8	0.66675	60.
as P_2O_5	2.546	0.588	0.4434	.....	....	.....	....
D. F. as P	0.6997	0.35535	0.04922	0.6505	93	0.2951	42.2
as P_2O_5	1.609	0.817	0.1132	.....	....	.....	....

A more recent paper by Cronheim and Meyer[11] gives figures for a normal child of about the same age as those investigated by ourselves. The absorption and retention in our cases are even higher than the results obtained by these authors (Table 15).

12. L. F. Meyer: Monatschr. f. Kinderh., vii, 104; Ergebn. der inn. Med. u. Kinderh., i, 317.

13. Keller: Ztschr. f. klin. Med., 1898-99, No. 36.

TABLE 15.—PHOSPHORUS METABOLISM IN HEALTHY CHILDREN (SEVERAL AUTHORS) APPROXIMATELY SAME AGES AND WEIGHTS

	Intake	Urine	Stool	Absorption	Per cent.	Retention	Per cent.
Rubner and Heubner,[9] child 7½ mos., as P_2O_5.	2.06	0.589	0.96	1.098	53	0.5079	24
Cronheim and Meyer,[11] child 6 mos.	2.184	0.967	0.733	1.451	66	0.484	22
	1.872	1.069	0.671	1.201	66	0.133	7

Keller, as well as Cronheim and Meyer and Rubner and Heubner,[9] have embodied a table of ratios of P_2O_5:N, in their papers. Our figures based on a similar intake of nitrogen show a reduced P_2O_5:N ratio in the urine (Tables 16 and 17).

TABLE 16.—RATIOS

	RATIOS P_2O_5:N.		
	Intake	Urine	Stool
Sch. I	1: 3.6	1: 4.5	1:10
Sch. II	1: 2.2	1: 5.4	1: 0.17
D. F.	1: 3.65	1: 3.4	1: 2

TABLE 17.—FIGURES FOR RATIO P_2O_5:N FOR HEALTHY CHILDREN (FROM SEVERAL AUTHORS) APPROXIMATELY SAME AGE AND WEIGHT AND DIET

	Intake	Urine	Stool
Rubner and Heubner	1: 2.1	1: 5.2	1: 0.29
Keller		1: 2.1 1: 3.4 1: 3.9	
Cronheim and Meyer	1: 2.1	1: 3.3	1: 0.7
Cronheim and Meyer	1: 2.4	1: 2.8	1: 0.7

SULPHUR METABOLISM

The literature contains but little of value on sulphur metabolism in children of this age; proper comparisons of only the output of sulphur can be made by utilizing the figures reported by Freund,[14] these findings, however, were obtained from the study of children suffering from gastro-intestinal disturbances (Table 18).

The absorption and retention of sulphur are both apparently very high, but as no literature exists bearing on this point, we can obviously make no comparisons as regards these results.

14. Freund: Ztschr. f. Physiol. Chem., No. 29. p. 54.

TABLE 18.—SULPHUR METABOLISM. DAILY AVERAGE

	Intake	Urine				Stool	Absorption	Retention
		Total S	Preformed SO_3 as S	Ethereal SO_3 as S	Neutral S			
Sch. I	0.521	0.1075				.0424	0.4786	0.3711
							85 %	71.2%
Sch. II	1.084	0.3020				.084	1.000	0.6985
							92.2%	60%
D. F.	0.5087	0.23235	0.1983	0.01262	0.02143	.07749	0.431	0.1989
			85 %	5.43%	9.57%		84.4%	39.1%

In Case D. F., neutral sulphur and ethereal sulphates were lower than the findings in Freund's[14] and Amberg and Morrill's[15] cases of children of about the same ages. We might deduce an increased oxidation of proteid tissue as evidenced by the high preformed sulphate output in its relation to total sulphur and neutral sulphur in the urine (Table 19).

TABLE 19.—ANALYSIS OF URINES OF NORMAL CHILDREN FOR SULPHUR CONSTITUENTS. (ALL IN TERMS OF S)

	Total S	Total Sulphates	Per Cent.	Ethereal Sulphates	Per Cent.	Neutral Sulphur	Per Cent.
Amberg and Morrill, child 5 mos	0.0747	0.0376	50.3			0.0371	49.7
Freund, child 6½ mos.	0.6717	0.570	86.6	0.0768	9.6	0.100	13.4
Freund, child 4½ mos.	1.032	0.773	75	0.0937	9	0.258	25

Referring to the work of Schwarz,[16] giving ratios of S: N in the urine, it will be seen from Table 20 that the excretion of S N in our cases is lower than those stated in the findings of this author (for a 5-year-old normal child), the amount of sulphur excreted being reduced in our cases.

TABLE 20.—SHOWING RATIO S:N

	Intake	Urine	Stool
Sch. I	1: 6.2	1:11.6	1: 5.6
Sch. II	1: 5.2	1:10.2	1: 0.9
D. F.	1:11.7	1:12.2	1: 3

GENERAL CONCLUSIONS

Most important in a consideration of the metabolism of amaurotic family idiocy is the stage of the disease and the general condition of nutrition of the patient under investigation. The two children studied by us were both in an early period of this insidious malady; their general

15. Amberg and Morrill: Jahrb. f. Kinderh., No. 69, p. 288.
16. Schwarz: Jahrb. f. Kinderh., 1910, lxxii, part 5, p. 549.

nutrition was good, muscular tissue still very well preserved, and an abundant panniculus adiposus was present. So good was the general health of the children, that during the periods of observation, in both the cases a gain of weight was noted. Thus Sch. gained in the four days of the first investigation 80 gm.; in the second period 30 gm.; Patient D. F. similarly gained 180 gm. In all these instances the nourishment was well taken, the diet consisting of milk diluted in Case 2, and undiluted in Case 1. The caloric intake was in excess of the accepted figures of Heubner (100 calories per kilo per day) to maintain proper nutrition.

From a perusal of the data before us, we are struck by the fact that absorption from the gastro-intestinal tract and retention within the body are normal or even better than normal for all the constituents determined (Table 21).

TABLE 21.—DAILY AVERAGE (PER CENT OF INTAKE)

	N	N	S	S	P	P	Cl	Cl
	..	Per Cent.	..	Per Cent.	..	Per Cent.	..	Per Cent.
RETENTION								
Sch. I ..	1.744	54.15	0.371	71.2	0.262	66.6	0.441	58.6
Sch. II ..	2.456	43.9	0.6985	64.4	0.6665	60	0.391	31
D. D. ..	2.772	47.5	0.1989	39.1	0.2951	42.2	0.948	62
ABSORPTION (PER CENT. INTAKE)								
Sch. I ..	2.9815	92.5	0.4786	91.7	0.3826	97.6	.....	....
Sch. II..	5.534	98.6	1.000	92.2	0.9222	82.8	.....	....
D. F. ..	5.6055	96	0.431	84.8	0.6505	93	.....	....

In view of the fact that this disease is so prominently characterized by a marked and generalized degeneration of nerve cells and nerve tissue, as proven by the very thorough and recent histologic and pathologic studies of Schaffer,[2] Vogt,[3] Brooks,[5] Sachs and Strauss,[6] and others, it would be interesting to discover in the excretions the chemical evidences of the degenerative process which we know is going on. This should be evidenced by some disturbance in the excretion of those elements which are so integral a part of nerve tissue, namely phosphorus and sulphur. In a paper dealing with the chemical analysis of the brain in two cases of amaurotic family idiocy, Mott[7] shows a very distinct change in the relative proportions of simple and neucleoproteins, the latter being diminished, and being replaced by proteins of a simpler composition and with an increased water content. (See Mott's table.)

Close scrutiny of our figures for the intake and output of phosphorus and sulphur does not disclose a marked disturbance in the metabolism

of these constituents. As has been stated, absorption and retention are unsually good and increased beyond normal, probably indicating a hypernormal anabolic function occurring at this stage of the disease. However, when one takes into consideration the very slow process of degeneration, extending over a period of months or years, and the very small amount of actual phosphorus and sulphur in the entire cerebrospinal system, one can understand why the daily elimination of these constituents would fail to be manifested in a study of this disease for short periods and with our present methods. It would be advisable, therefore, to study the disease at intervals during its entire course, both in its earlier stages when anabolic changes apparently predominate, and in its later stages when degenerative and catabolic processes play the important rôle.

TYPHOID FEVER IN INFANCY. AN ANALYSIS OF SEVENTY-FIVE CASES

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In a contribution published about ten years ago in collaboration with Dr. Maurice Ostheimer,[1] a study was made of all the published cases of typhoid fever occurring in the first two and one-half years of life, so far as we could find references to them. In this report we included synopses of 18 cases, the majority of which had been under my personal care; the remainder being unpublished cases in the practice of colleagues. To these 18 cases as a nucleus I have added such others as have come under my observation in hospital or private practice, or are found in the records of my colleagues at the Children's Hospital. The total equals 75 cases in all, more than one-half of the number having been under my personal care. The series is much larger than any individual one previously published, as far as I am aware, and it is hoped may be correspondingly useful.

The possibility of making an entirely complete percentage analysis is interfered with by various circumstances, such as lack of accurate medical knowledge of the onset, especially of the hospital cases, the meagre character of a few of the hospital case-histories, the lack of details obtainable in some of the cases seen in consultation, etc. This does not hinder, however, the drawing of serviceable general conclusions, and even the giving of many statistical analyses.

Age of the Patients.—The age limit was fixed at two and one-half years. This is in a way arbitrary, as the termination of infancy is better placed at two years, the first six months of the third year belonging to the period of early childhood, which extends to the age of six years. The limit of two and one-half years was adopted chiefly because in the first half of the third year the general characteristics of the second year of life are still well marked; partly because after two and one-half years the cases of typhoid fever multiplied so rapidly that the number became inconveniently large, and partly because in the former article on this

1. Griffith, J. P. Crozer and Ostheimer, M.: Am. Jour. Med. Sc., November, 1902.

subject already referred to this age limit had been chosen. Any references in this contribution to "infancy" will therefore indicate the first two and one-half years of life, "early childhood" denoting the time from the close of this period to the age of six years.

In the present series 9 of the patients (12 per cent.) were one year or less of age, the exact figures being: three months, 1 case; five months, 1 case; seven months, 1 case; nine months, 2 cases; ten months, 1 case; eleven months, 2 cases; one year, 1 case. From this age up to and including that of two years there were 36 cases (48 per cent.); and 30 cases (40 per cent.) of over two years up to two and one-half years. An unduly large proportion were recorded as "two years" or "two and one-half years" old—12 cases and 13 cases respectively. This is because these figures are in a sense an approximate statement on the part of the parents, who failed to give the exact number of months. This applies with especial force to the earlier cases studied. In the later ones the case-histories include a statement of the date of birth, and the criticism, therefore, holds good only in a small proportion.

Race.—Sixty-five (86.67 per cent.) of the children were white; 10 (13.33 per cent.) colored.

Family History.—In only 16 cases (21.33 per cent.) was the disease existent in other members of the family—one of these being five months of age, one nine months, one fifteen months, one seventeen months, one eighteen months, one twenty-one months; one twenty-three months and the remainder two years or over. This indicates that the statement which has sometimes been made, that it is particularly in family epidemics that infants are attacked, certainly does not apply to this series, since in 78.66 per cent. of the children no other case occurred in the family.

Onset.—The *duration of the onset* was determined by the development of spots when this was known, or in some cases by the evident attaining of the fastigium before the appearance of spots was noted. In cases first coming under observation on what was stated to be the eighth day of the disease the duration could not be determined accurately, as the temperature seemed in nearly all of these to be already at its height: and if the roseola was already present, as was true in nine instances, it could be concluded only that the onset had not lasted *over* a week; it might readily have been less than this. Some instances of early observation gave positive evidence of the short duration possible. Thus we

see, as marked by the fever reaching its height, the onset lasting in 4 cases, two days; 3 cases, three days; 5 cases, four days; 9 cases, five days; 11 cases, six days or less; 12 cases, seven days or less. In at least 44 cases, therefore — 58.67 per cent. of the total number — the onset lasted not over seven days, and in at least 21 (28 per cent.) not over five days. In the remaining cases the date of the first observation was not early enough to allow of conclusions.

The *method of onset* could be studied in fifty-nine patients. In the remaining sixteen there were not sufficient data to allow of conclusions being formed. There was reason to believe the onset *sudden* in at least twenty-one of the fifty-nine (35.59 per cent.). In these the symptoms came on in force on the first day, and the child was clearly acutely ill. In sixteen others (27.12 per cent.) the onset could be called *rapid*. These together make thirty-seven of the fifty-nine cases (62.71 per cent.) in which there was a rapid development of very decidedly threatening symptoms. In twenty-two cases (37.29 per cent.) the onset appeared more gradual.

We are then justified in concluding that there is a peculiar tendency in infancy for the onset to be sudden or rapid in its development and short in its course.

The symptoms of the onset may be considered in some detail, as shown by cases where statements were sufficiently complete to permit of analysis:

Fever.—The reports show this mentioned in fifty-seven cases. By fever is meant in most instances such a degree of elevation of temperature as the parents could themselves recognize, without using a thermometer, which would naturally have shown fever in all cases. In those cases where early study was possible the temperature was found to rise rapidly, reaching its height much sooner than in adult life, as has already been pointed out. Probably the majority of cases would show the fever at its height in from three to four days if observation from the beginning had been possible.

Diarrhea.—There is a much greater tendency to diarrhea during the onset in infancy than is seen in typhoid fever in early or later childhood. In forty-three cases (57.33 per cent.) this symptom was reported. In seven others there was constipation, and in seven the bowels were undisturbed. In the remaining no statement is made and diarrhea doubtless was not a prominent symptom if present.

Vomiting.—This is a symptom to which infants are, of course, predisposed from slight causes. It is surprising to observe how frequently it was reported as an early symptom of typhoid fever at this period—twenty-six cases in all (34.67 per cent.). In the others no mention is made of it. In a few it occurred but once or twice and may have been accidental, but in the remaining it was evidently a marked symptom, and in some was the principal one.

Malaise or prostration was stated to be present, or this is readily gathered from the history, in but eighteen cases. There is no question, however, that decided weakness and sensation of illness occurred in a decidedly larger number of cases than this.

Headache was noted in fourteen patients (18.67 per cent.), all of at least 2 years of age. How frequently it was present before this age cannot be determined.

Loss of appetite was reported in twenty-five cases (33.33 per cent.); by which was probably meant a very decided impairment of appetite. Doubtless it existed in others in a less marked degree.

Cough was not frequent during the onset, but eighteen cases (24 per cent.) having it reported.

Epistaxis is noteworthy by its infrequency, it having been seen but four times (5.33 per cent.) during the onset. This is in marked contrast to the condition in adults.

Distended or tympanitic abdomen was also infrequently mentioned; only five cases in all. Probably others were overlooked, or no statement made; but it clearly is not a common prodromal symptom.

Abdominal Pain or Tenderness.—Reference was made to this in but twelve cases (16 per cent.), all among the older infants. Like headache, it may have been existent more frequently; but it was certainly not a common symptom, since *fretfulness* is reported in but eleven (14.67 per cent.). Had pain in any portion of the body been a prominent early symptom there would certainly have been more crying recorded.

Unusual drowsiness was mentioned nine times (12 per cent.), in two instances the children, of 17 and 18 months, sleeping nearly all the time.

Convulsions were reported in but three cases (4 per cent.); one on the first and second days, one on the second, and one having convulsions several times during the onset. It is a striking fact that this symptom is so unusual during the onset of typhoid fever in infancy—in sharp contrast to the condition seen in pneumonia, scarlet fever and some other acute diseases.

Apart from convulsions, *unusual nervousness* was reported in only four instances; *unusual restlessness* three times, and *screaming* in two cases. These last two showed *rigidity* as well, and the onset was distinctly that of meningitis. In one other case there was *early delirium*. Among the other less common symptoms recorded may be mentioned *sore throat*, one case; *nausea*, two cases; *decided thirst*, one case; *pain in the back*, two cases; *unusual apathy* or *stupor*, three cases.

GENERAL CONCLUSIONS REGARDING THE ONSET

The onset of typhoid fever in infancy is of decidedly shorter duration than later, its length averaging perhaps three to four days before evidence of the fully developed attack is present. The attack usually comes on rapidly and is often sudden, only about one-third of the cases showing a slower appearance of symptoms. These symptoms consist chiefly of fever, diarrhea, vomiting, prostration, headache, loss of appetite; less often of cough, fretfulness and abdominal pain. The temperature rises rapidly, diarrhea is more common than in childhood, vomiting is a symptom decidedly more frequently seen than later, and loss of appetite is often observed. Prostration is seldom marked. Cough, abdominal pain and distention are comparatively infrequent, and epistaxis is rare.

SYMPTOMS OF THE DEVELOPED ATTACK

These may be said to date certainly from the time the roseola appears, or, in any event, from the time the fever has reached its height and the disease is thoroughly under way. Apart from the nature of the onset already described, the general course of the disease in infancy, although subject to great variation, would appear on the whole to have definite characteristics. General conclusions can best be drawn after giving a more detailed description of the symptoms seen in the seventy-five cases under consideration.

Digestive Symptoms.—Coated tongue was recorded in thirty-five cases (46.67 per cent.) and was probably present, but not mentioned, in many others. In only one is the tongue described as dry and fissured. The lack of tendency to the appearance of the tongue characteristic of the typhoid state as seen in adults is, therefore, very marked in infancy, so far as this series indicates.

Sore throat was reported in eleven cases, shown by redness of the pharynx or tonsils. In the majority there is no record regarding the symptom and conclusions are impossible.

Loss of Appetite.—It is noticable how seldom this was observed in may series—only five cases (6.67 per cent.). Although probably present in others, but not recorded, it is clear that decided loss of appetite must have been uncommon. This depends, perhaps, to a considerable extent on the fact that at this age a lesser degree of discrimination as to taste, or of less determination regarding it, made the patients quite willing to take milk in order to allay the thirst which was often present.

Vomiting was a not infrequent symptom. I find it mentioned in twenty-seven instances of the seventy-five (36 per cent.). In at least eight of these, however, it happened only once or twice after the onset, and in a number of others was insignificant and no more than children of this age, with any illness, are liable to exhibit. In no case was it a threatening symptom, and on the whole it is to be regarded as not one of either great frequency or severity.

Diarrhea.—As would appear from this series, this is much more frequent in infancy than in either early or later childhood. I find it recorded in fifty-eight of the seventy-five (77.33 per cent.). These figures may be misleading to a certain extent, because, at this age, and in the first year especially, the bowels are naturally softer and more frequently moved than later, and a very slight increase of this condition might be called diarrhea and yet not really be this. A study of the case-reports, however, in which the character as well as the frequency of the stools is described, shows that this doubt can attach to but few of the cases. In not many was the diarrhea severe enough to be a matter of importance; but it is certainly to be regarded as a common symptom. In fifteen cases (20 per cent.) there was no diarrhea, and in three of these the bowels were constipated. In two instances no record has been made.

Abdominal Distention.—Under this heading, or that of tympanites, is the record of forty-three cases (57.33 per cent.). The observation is misleading to a certain degree, some infants having probably a distention from rachitis, or other previously debilitating cause. On the other hand, there has probably often been the failure to record the presence of moderate distention. It remains evident that abdominal distention is a symptom frequent in infancy—more so in my experience than in children after this period; yet when present it was only exceptionally a symptom causing distress or requiring treatment. In only four cases is it distinctly stated that the abdomen was not distended. In the remaining no note was made, and no conclusion is possible.

Respiratory Symptoms.—Bronchitis was so frequently present that I have put it among symptoms rather than complications. Râles in the lungs were recorded in twenty-nine cases, although often only few and scattered. Cough was mentioned in fourteen and undoubtedly was present slightly, but overlooked or ignored, in more, as the disproportion between cough and râles is evident. In some of the cases of cough no râles were recorded, and in others the lungs were reported as negative. In at least thirty-seven cases (49.33 per cent.) there were observed either râles or cough, or both. In twenty (26.67 per cent.) there were no evidences of bronchitis noted. In the remaining no record at all was made. We are certainly justified in concluding that tracheobronchitis is a symptom quite common in infancy, but that it is rarely one of importance.

Rhinitis was mentioned in but one case.

Epistaxis after the period of onset was recorded in three instances only (4 per cent.). This is in decided contrast to the frequency of epistaxis in adult life; or even to that of later periods of childhood, where it is generally, in my experience, less often seen than in adults.

Rapid or labored respiration was reported in five cases, dependent in four on prostration and in one on bronchitis.

Heart and Pulse.—There is little to be said in this connection. A feeble or rapid pulse is distinctly spoken of in fourteen instances, but was undoubtedly present in decidedly larger number. A rapid pulse-rate attending high fever is, however, of frequent occurrence in infants, no matter what the disease, and it was only in those of the series who were severely or fatally ill that the symptom became one of importance. Treatment for circulatory disturbances was rarely required. A pulse-rate of 130 to 160, with a temperature of 103 to 104 F., was a common figure in cases of moderate severity.

Nervous Symptoms.—With the exception of more or less prostration, nervous symptoms were, as a rule, little marked in the cases of this series. There was little of the evidence of the typhoid state so common in adult years, and even the apathy characteristic of early and later childhood was not a prominent feature. Oftener, perhaps, there was decided restlessness, irritability and fretfulness, and in a few cases the signs of nervous excitement were still more marked, as represented by convulsions, rigidity and the like. More in detail, the symptoms seen were as follows:

Prostration was reported as evident in twenty-one cases (28 per cent.), generally very decided; and was present without doubt to a certain extent in many more. The mildest cases, however, showed little of it

and the children remained in good general condition. Its degree appeared to be proportionate to the general severity of the attack.

A condition of *dullness, apathy, or listlessness* was recorded in but seven instances; *unusual drowsiness* in one; a *stuporous condition* in four; *unconsciousness* in one, and *"mind not clear"* in two. This bears out the belief I have previously expressed, that the ordinary adult nervous symptoms are almost always wanting. Only in one case was there a condition closely resembling the adult type in this respect.

On the other hand, evidence of *nervous excitation* was present perhaps oftener than at later periods in early life. This was shown by *increased restlessness, nervousness* and especially, *irritability* and *fretfulness,* and was present in at least twenty-seven cases (36 per cent.), and probably in others in which no direct reference was made to it. In a few the nervous manifestations of this class were still more marked, at least at some time during the fully developed attack. The records showed *convulsions* at this time in five instances; *rigidity* of the neck or limbs in three; and *tâche cérébrale* in two. In three cases symptoms distinctly suggesting meningitis were present. The severity of the nervous symptoms appeared to exhibit little, if any, relationship to the height of the temperature. This is not in accord with the views expressed by some writers. Very few references to *pain* are made, and, as far as could be determined, the attack was in most cases not of a painful nature, as is true of typhoid fever at any age. In one instance there was pain on moving the neck.

On the whole, it may be said of nervous symptoms at this early period of life that they show themselves oftener through evidences of excitement than of depression, and, although probably more frequent than in early or later childhood, are not a very prominent feature.

Temperature.—It is almost impossible in a series of cases as large as this, with a symptom so variable as temperature, to formulate any specific classification. As already pointed out, the temperature during the onset rises rapidly and reaches its maximum probably by the third to the fifth day in most instances. It then continues *high,* from 103 to 105 F., being little influenced by bathing, for a variable time in the average case; perhaps a week or a little longer. In other cases the temperature is *moderately* but steadily elevated at from 101 to 103 F. during the early period. In both these groups one of two changes very commonly occurs; either, first, there is a diminution in the average height of the temperature, which, however, still runs *steadily* with daily variations of from

1 to 1½ degrees; or, second, the temperature becomes decidedly *irregular*, with greater falls after bathing, or occurring independently of this, and without any discoverable cause of irregularity or fixed relationship to the time of day. In still another large class of cases the temperature is more or less *irregular* and *uncharacteristic* during all the period of observation, and either, in general, moderate or averaging high.

The *method of fall* varies greatly. Sometimes there is a rapid fall; sometimes a gradual descent of the curve as a whole to normal; sometimes at first a gradual fall ending in a much more rapid one, with no marked remissions. In other cases decided remissions are present. These generally do not exhibit morning fall and evening rise, as in the adult picture, but occur more irregularly. It is very exceptional, indeed, to see a curve of the adult type.

The duration of the fall, too, is very different from that observed in adults. Frequently three or four days from the time a decided tendency to a lesser elevation first shows itself will find the temperature normal. In others six or seven days are required. Not infrequently the fall of temperature is almost critical, occupying one, or sometimes two, days. Slight recrudescences occur readily, but on the whole not frequently. Only occasionally one sees a long persistence of irregular, slight fever, very similar to the condition at times observed in later periods of childhood and in adult life.

The following synopsis gives a more detailed statement of the course of the fever and its duration in the cases analyzed. In 6 cases a record of the temperature was lacking. The remaining 69 may be classified as follows:

Course of the Temperature.—Temperature steadily high (103 to 105 F.), with little daily variation, sometimes followed by irregularity later —31 cases (44.93 per cent.).

Temperature moderate (101 to 103 F.), steady, with little variation, at least early—11 cases (15.94 per cent.).

Temperature of an irregular type throughout, with an average either high or moderate—27 cases (39.13 per cent.).

The *character and duration of the fall* was studied in 48 cases. In the remaining various circumstances interfered with this. These 48 cases may be classified as follows:

Fall gradual, 17 cases (35.42 per cent.).

Fall more rapid, 31 cases (64.58 per cent.).

In these more rapid cases the fall lasted one day (critical), 8 cases; two days, 7 cases; three days, 8 cases; four days, 8 cases.

In 2 of the cases with gradual fall the curve was of the remittent type characteristic of the third stage seen in adults.

Total Duration of the Fever.—The following synopsis gives in condensed form the duration of the attack, as evidenced by the duration of fever. As in nearly all series of cases of typhoid fever at any age, there is often lacking here an absolute accuracy. This is due to the impossibility in some cases of determining the exact date of onset. On the whole, however, the figures may be considered fully as accurate as those obtained from series of patients of older age.

(1) Duration undetermined on account of the occurrence of early death in the course of the fever, complications prolonging it, etc.—27 cases.

(2) Duration of the attack determined in 48 cases as follows: Seven days, 1 case; eight days, 1 case; ten days, 2 cases; eleven days, 2 cases; twelve days, 3 cases; thirteen days, 5 cases; fourteen days, 3 cases; fifteen days, 5 cases; sixteen days, 4 cases; seventeen days, 3 cases; eighteen days, 1 case; nineteen days, 4 cases; twenty days, 2 cases; twenty-one days, 3 cases; twenty-two days, 4 cases; twenty-five days, 2 cases; twenty-six days, 1 case; twenty-seven days, 1 case; thirty-two days, 1 case. It will be seen, then, that the duration of the fever in these 48 cases was over three weeks in 9 instances (18.75 per cent.), and of three weeks or less in 39 instances (81.25 per cent.), 17 of these (35.42 per cent.) lasting but two weeks or less. In one of the cases classified as undetermined, the fever continued for thirty-six days, and in another for fifty-seven days. Whether this depended on undiscovered complications or on persistence from other cause could not be accurately decided.

Cutaneous Symptoms.—Typhoid Roseola.—This was recorded in 48 of the 75 cases (64 per cent.), and it is practically certain that repeated systematic search would have shown it present in more. Sometimes the spots were very numerous, widespread, and appeared in crops; in others they were but few in number. There seems to be no difference from later life in this respect. The exact *time of the appearance* could be determined in a few cases only. In 1 instance the spots developed on the fourth day, the onset here being sudden and its date clearly known. In 5 cases the date of appearance could be fixed at the sixth day, and in 8 other cases, first examined on the sixth day, the rash was already present. In

4 cases first examined on the seventh day, the rash was already out, and in 1 other it could be fixed at the seventh day. In 2 cases the date was certainly the eighth day, and in 7 first examined on this day the rash was already developed. How much earlier it had appeared could not, of course, be determined. In 4 cases the rash was first discovered on the ninth and in 2 on the tenth day. In the remaining cases, for the most part, the rash was found when the child was first seen at later periods in the disease.

We may conclude, then, that in the first two and one-half years of life, as shown by this series, there is a decided tendency for the rash to develop much earlier than in adult life, somewhere from the fourth to the sixth or seventh day, there having been at least 14 cases, *i. e.*, 18.67 per cent. of the total number, or 29.17 per cent. of the 48 cases, in which it developed on or before the sixth day. The early appearance of the rash probably corresponds to a certain extent with the shorter duration of the onset characteristic of so many cases at this time of life. There are, however, exceptions, and the rash may first appear on the eighth or ninth day and even later. Probably, in most of the cases in which the rash seemed to have been later in developing, the spots were few in number and the earlier ones were overlooked.

Of other cutaneous manifestations *herpes* was observed in 2 instances and *petechiæ* in 2.

Splenic Enlargement.—The determination of this symptom is always more or less unsatisfactory in infancy, owing to the common abdominal distention and to the voluntary resistance offered. More frequent examination would surely have revealed enlargement in more cases. As it was, I find the record of enlargement of the spleen in 40 cases (53.33 per cent.). In 4 of these this was determined only by percussion and in 1 only at autopsy; but in all, or nearly all, the others by palpation, since this was the only method of physical examination relied on. Data regarding the time of the discovery of the enlargement were collected, but are not sufficiently detailed to be of value. It may be said that, as a rule, the splenic enlargement was observed at the same time as the roseola, or a little later. In 26 cases it is stated that no enlargement was found, and in 9 no record at all was made.

Blood.—Widal Serum Reaction.—A few of the earlier cases antedated the time when the employment of the Widal agglutinative reaction became common. A test was made in all but 9 instances. Of the remaining 66 cases, 62 gave a positive reaction and only 4 a negative one. The

4 negative cases exhibited typical symptoms in other respects. We have, therefore, 82.67 per cent. of the 75 cases giving a positive Widal reaction, or 93.94 per cent. of the 66 cases examined.

Leukocytosis.—In 43 of the children a leukocyte count was made. The result sustained the diagnosis in nearly all instances. A detailed account would occupy too much space. Grouping them, there were 4,000 to 5,000 per c.mm., 2 cases; 5,000 to 6,000, 4 cases; 6,000 to 7,000, 3 cases; 7,000 to 8,000, 5 cases; 8,000 to 9,000, 11 cases; 9,000 to 10,000, 4 cases; 10,000 to 11,000, 5 cases; 11,000 to 12,000, 2 cases; 12,000 to 13,000, 1 case; 14,000 to 15,000, 3 cases; 16,000 to 17,000, 1 case; 18,000 to 19,000, 1 case; 20,000 to 21,000, 1 case. In 36 of the cases the number of leukocytes did not exceed 12,000, and in only 7 was it over this figure. In one of these pneumonia was present as a complication, and in another pyelocystitis; in the others no complication could be discovered.

Urine.—Examinations are recorded in 38 cases only. Of these, 12 showed albuminuria and 26 none. In 6 of the 12 there was also the presence of hyalin and granular casts. In 4 of the 6 they were but few in number, but in the remaining 2 more numerous. In 1 case albuminuria depended on pyelocystitis. As so many of these cases of typhoid fever in infancy are of the severe type, albuminuria might reasonably have been expected to be more frequent than it was.

GENERAL CONCLUSIONS REGARDING THE SYMPTOMS OF THE ATTACK

The fully developed attack of typhoid fever in infancy shows many *digestive symptoms.* Coating of the tongue is of common occurrence; dryness and fissuring are exceptionally rare. Redness and swelling of the throat would probably be found frequent if examinations were systematically made. Decided loss of appetite is uncommon; vomiting is comparatively frequent, although often only occasional and seldom severe. Diarrhea is certainly much more common than in early childhood, being seen in decidedly the majority of cases, but is seldom severe enough to demand specific treatment. Abdominal distention is frequent; probably more so than at later periods of childhood, but is seldom distressing.

Of respiratory symptoms bronchitis is common, but seldom a matter of importance, and epistaxis is rare. The *heart and pulse* are seldom much involved and only in the severest cases, a rapid pulse-rate being the natural phenomenon in typhoid fever at this time of life. *Nervous symptoms* are, on the whole, not marked, those of depression being

decidedly less frequent than those of excitation. The typhoid state of the adult is very exceptional. Prostration is not often great, but moderate irritability and fretfulness are frequently seen. Only occasionally does the disease simulate a meningitis.

The course of the *temperature* is uncharacteristic; a temperature steadily high or moderate, and later often irregular, being of frequent occurrence, and almost as frequent is one which is irregular from the beginning. Not only is the initial rise of temperature rapid, but the fall is so also in many cases, an almost critical fall being sometimes seen, and still oftener one which requires only three or four days for normal to be attained from the time the first decrease of fever shows itself. The morning fall and evening rise of the third period of the adult is very exceptional in infants. The total duration of the fever is three weeks or less in the great majority, and in at least one-third of the cases only two weeks or less.

The typhoid *roseola* is probably as common as in adults, but appears earlier, oftenest from the fourth to the sixth day. *Splenic* enlargement is found in at least one-half the cases. The *Widal* reaction is as characteristic as in adult life and leukocytosis is usually absent, in spite of the fact that in infancy many outside causes readily disturb the leukocyte count. The *urine* often shows albuminuria, with casts in a considerable number of cases.

COMPLICATIONS

These are of various sorts and encountered not infrequently, 31 patients (41.33 per cent.) showing complications of some kind. They may be enumerated as follows: Diphtheria, 9 instances; measles, 3; pneumonia, 7; pertussis, 1; jaundice, 1; intestinal hemorrhage, 1; conjunctivitis, 1; aphthous stomatitis, 1; ulcerous stomatitis, 2; necrosis of the jaw following ulcerous stomatitis, 1; parotitis, 2; (1 suppurative); purulent otitis, 8; pyelocystitis, 1; furunculosis, 5; abscesses, viz., ischiorectal, 2; submaxillary (glands?), 2; buttock, 1; sacral region, 1; scapular region, 1; fingers, 1; abdominal walls, 1. There will be noticed here especially the tendency to suppurative processes, evidenced in 19 of the 75 patients (25.33 per cent.). Nephritis has been mentioned earlier under symptomatology.

RELAPSE

This occurred in 3 instances, with a possible 4th. In the latter, development of measles prevented the accurate determination of the question. In the other 3 the intervals between the first and second attacks were

respectively fourteen, fifteen and five days. In the last case some uncertainty existed on this point, as the presence of suppurative processes about the end of the first attack may have prolonged this unduly.

DIAGNOSIS

This must be considered carefully, since the disposition has often been shown on the part of many physicians to question its correctness in cases supposed to be typhoid fever at this time of life. There were a number of cases entered upon the records of the Children's Hospital as typhoid fever which I have rejected as not conclusive. Of the 75 reported, 62 cases, as already stated, gave a positive Widal serum-reaction.. In at least 48 instances the typhoid roseola was present. In a considerable number, also, as already detailed, there was enlargement of the spleen, a very decided history of others in the family suffering from typhoid fever or an absence of leukocytosis. Taking a positive Widal reaction as a proof of the existence of typhoid fever, we have only 13 cases of the 75 not showing this. Of these 13 only 4 gave a negative reaction, and later examinations would probably have given a positive result. In the other 9 a test was not made. In all but 3 of the 12 the diagnosis was confirmed by the presence of the typhoid roseola, often with splenic enlargement. In 2 of the exceptions, in which neither roseola nor positive Widal reaction was recorded, there were, in addition to other suggestive symptoms, the presence of typhoid fever in other members of the family, and in 1 of these the post-mortem lesions characteristic of the disease.

Lest any question be raised about the reliability of the Widal reaction in these cases as a diagnostic sign, I may add that in nearly all cases giving the reaction other very positive confirmatory signs were present. In all but 23 of these the typhoid roseola was present also. In 11 of these 23 the diagnosis was confirmed by the leukocytic count; in 1 by autopsy; in 1 by the family history; in 1 by the occurrence of well-marked relapse; and in 1 by enlargement of the spleen. This leaves but 8 cases, and in 3 of these the obtaining of 2 positive Widal reactions seems sufficient proof. No account is being made in this connection of the symptom-complex in other respects, although this naturally must have weight.

Probably in any group of cases of whatever age some errors in diagnosis will occur, but the present series can, I think, be rightly questioned

no more than a series in older patients; indeed, probably with less reason on account of the special care which has been taken to avoid the occurrence of error as far as possible.

Post-Mortem Lesions.—Only 3 autopsies were obtained—in children of three months, five months and twenty-seven months, respectively. The appearances were similar in all. There were found enlarged spleen and mesenteric glands, with swollen Peyer's patches and solitary follicles. In 2 instances there was very superficial ulceration, and none at all in the other. This confirms the prevailing views regarding the anatomic lesions of typhoid fever in infancy.

PROGNOSIS

With regard to the *severity in general* of typhoid fever in infancy, the records show 8 very mild; 11 which may be called mild; 23 moderately ill, perhaps as much so as the average case in childhood; 33 which must be called rather severe. These estimations are, for the most part, based upon the written case-histories, from which the forming of a conclusion is difficult. Still, it is evident that the disease was of a rather severe type in the cases reported.

This is borne out, too, by the mortality figures, since 12 of the patients died; a mortality of 16 per cent. The ages of these 12 patients were respectively three, five, seven, fourteen, fifteen, eighteen, nineteen, twenty-one, twenty-seven, twenty-eight months, each 1 case; and thirty months, 2 cases. One of these patients should fairly be excluded from the list, as death resulted from pneumonia with measles, which appeared after two weeks of apyrexia. Two others developed diphtheria just as the course of the typhoid seemed to be closing; yet there is no good reason to exclude them, since the attack of typhoid fever undobtedly rendered death from diphtheria much more likely to occur. However, even omitting all 3, there remains a mortality of 12 per cent., a figure decidedly higher than I have found in early childhood, the most favorable age, and fully equal to, if not greater than, that which we may reasonably look for in later childhood. The cause of death in the 12 cases depended, in part at least, on complications, these being pneumonia in 2 cases and diphtheria in 3. In 7 cases no complicating condition could be discovered, except 1 instance, where numerous furuncles perhaps added to the great prostration upon which death followed. In the others death appeared to be a direct result of the disease itself.

TREATMENT

Little discussion of this topic is required. The treatment employed was in every instance symptomatic. The use of hydrotherapeutic measures was systematically followed. Tubbing was usually preferred to sponging, as it was both more effective and less trying to the patient. Occasionally packing answered well. Cold baths were never given, the water used being of a temperature of 90 to 100 F. Diarrhea sometimes needed treatment, and cardiac stimulation was required in the severer cases. The diet, as a rule, was largely of milk, as being best suited for patients of this early age. Often cereal gruels were also administered when milk was deemed insufficient, and sometimes broth, beef juice and albumen water. In no instance was there evidence of any deleterious symptoms following a milk diet, as some writers have claimed is likely to occur. Indeed, in some cases where no milk had been given for a time, improvement occurred when a milk diet was resumed, while in others unfavorable symptoms did not disappear after milk had been stopped. There seemed, in fact, to be no relationship between typhoidal toxemia and the diet.

DISCUSSION

DR. HAND asked Dr. Griffith if he had attempted to classify the case he reported so as to be able to tell how many were under 1 or 2 years of age. The conclusions reached by Dr. Griffith bore out his own experience; the general type of the disease they had been able to readily recognize, as a rule, ran a short course but with a high temperature of from 103 to 105 F. The average duration of these cases did not differ so much from that occurring in the older children. The cases of long duration were those with a lower temperature, from 101 to 102.5 F. It should be remembered that typhoid fever occurring in infants differed from the typhoid fever that occurs in adults; among the latter the temperature might be from 101 to 102.5 instead of 103 or 105 and coming down rapidly. The diagnosis of typhoid fever by means of the Widal test in infants he believed to be as easy as the diagnosis in adults; in fact he thought it had more value in infants than it had in adults because, in the latter, there was a greater possibility of the patient having had a previous attack and he gave what he considered a beautiful illustration of this. A woman was admitted to the surgical ward with a diagnosis of appendicitis. The Widal test was made and was positive. It was learned that she had typhoid fever six years previously, when she was transferred to a gynecologist as a case of pelvic abscess. If there had not been a previous history of typhoid fever in this case the results of the Widal test would have given them a sense of false security.

Dr. Hand said he was surprised to hear of the high mortality that Dr. Griffith said occurred in infants because he thought that better results were obtained among them. Sixteen per cent. mortality was pretty high he thought. There were cases of very sudden onset, with a distinct history of previous good health of one day; then within three days there would occur a high fever, one that went to the maximum; sometimes the initial infection went hard with the infant and, there-

fore, up went the mortality rate. With regard to nose bleed, Dr. Hand could not recall an instance of it occurring among infants, certainly not in his wards. He knew no explanation of it. As a rule the diagnosis was comparatively easy, and the Widal test merely confirmed that diagnosis in practically all the cases. It should be used far more frequently in infants than in adults especially in those abortive cases of typhoid fever; the disease certainly was not recognized as frequently as it should be. Many of the cases at first were attributed to "cold" or an enteritis. Dr. Hand reported the histories in brief of two sisters who were admitted to the hospital, both with temperatures of 103 F. In one the Widal reaction was always negative. In the other when the temperature became normal, as it did in a few days, there was a positive reaction. The value of this was especially shown in a community where typhoid fever was prevalent. Instead of twenty-one out of twenty-four beds being occupied by patients with typhoid fever they now only occasionally had a case.

DR. MORSE said that Dr. Griffith's paper had covered the ground very thoroughly. His experience had been smaller that Dr. Griffith's, but what he had seen led him to agree with Dr. Griffith's conclusions regarding the sudden onset, the quicker fall of the temperature and the greater severity and mortality of the disease. It seemed to him that the cases he had seen did not require the Widal test to make a diagnosis. The relative slowing of the pulse was less evident in infancy and hence the relation of the pulse to the temperature less important than in childhood and adult life. Leukopenia was of the same importance in infancy as later.

DR. CHURCHILL said he could not agree with what Dr. Hand had said about the diagnosis in infants being such an easy thing; he thought it was an extremely difficult matter. Making a blood-culture would nail the diagnosis quicker than would the Widal test. An examination of the blood in young children in making a diagnosis of typhoid fever was very important. Dr. Morse spoke of leukopenia being of greater aid than the Widal reaction but a cultural examination of the blood was, in his opinion, the only way in which they could make sure that they were dealing with a case of typhoid fever. Dr. Griffith said bronchitis occurred in 47 per cent. of the cases. Dr. Churchill had not seen as many cases but bronchitis had occurred more frequently than that among his; when the chests of these infants were examined carefully, bronchitis would be found in from 90 to 95 per cent. at some time during the disease. This complication was not always severe, however. With regard to the leukocyte count, Dr. Churchill asked in what stage of the disease the examination was made.

DR. KERLEY asked how these infants were fed.

DR. GRIFFITH replied that he could not make an exact answer because he had no records, but they were fed mostly on a milk diet. It was the practice of most of them to use a milk diet when treating infants at the Children's Hospital, but sometimes they added some other food such as broths.

DR. KERLEY said that the only way and the best way to bring up a high mortality rate was to feed these infants with typhoid fever, milk. In twenty-four years of active work in the practice of medicine, and particularly among children and infants, he had learned that milk was absolutely contraindicated in typhoid fever.

DR. GRAHAM said that his experience with infantile typhoid fever corresponded largely with what was stated by Dr. Griffith, but there were one or two particulars in which he differed. He had always believed that the mortality rate in early childhood was comparatively low, something below 16 per cent.

Dr. Hand stated that there was little typhoid fever in Philadelphia and Dr. Graham recalled the time when in a certain hospital the wards were filled with these cases; whereas this year there had not been a single case there. He had recently seen, however, in Philadelphia three cases in ten days, one infant 7 months old, one between 2 and 3 years and the third child 7 years, and they occurred in a section where they had a splendid water-supply. In two of the three cases there had been previously a case of typhoid in the houses in adults. Children, and especially infants, should be guarded against infection in such instances; they commonly get the infection through personal contact with the older individuals in the household and this should be guarded against.

DR. HEIMAN said that he had found it rather difficult to make a diagnosis of typhoid fever in children unless in the midst of an epidemic, and especially in the summer time with the usual occurrence of gastro-intestinal diseases. He made it a practice always to have the Widal test made in a suspicious case. With regard to blood-cultures, it was extremely difficult to get into the veins of these little children. Probably in time with an improved technic we will be enabled to do this.

DR. ADAMS said that some years ago he had called attention to the prevalence of typhoid fever among infants, a fact which was not generally recognized. He also called attention to an epidemic that occurred in the Foundling Hospital which was under his supervision. Here there was a nurse caring for ten babies; eight out of ten were stricken with typhoid fever. The nurse was supposed to be under the weather but she would not give up her work. She was sent to another hospital where she died of typhoid fever. Eight out of the ten babies had contracted typhoid fever, and one died from intestinal hemorrhage.

So far as the mortality was concerned, Dr. Adams said he would like to repeat what Dr. Osler had said to the late Dr. Atkinson. The latter stated that the mortality was higher in Washington than it was in Baltimore and in Dr. Osler's reply he made the statement that they were dealing more with hospital cases and not with those encountered in private practice. Between these two classes there was a marked distinction. Infants and young children in the hospitals were always in worse condition when they were admitted, their environment was worse; when brought to the hospital they were in a far worse condition than were those seen in private practice at the same period of the disease.

With regard to the Widal reaction and blood-cultures, Dr. Adams said he was glad to hear what Dr. Heiman had to say. In one epidemic the best assistants he could get in this country hesitated to take blood-cultures in young infants; they would not take chances in babies under 7 months of age.

Similar to Dr. Hand, he had had the greatest difficulty during the past winter in getting enough typhoid cases to illustrate the disease to a class of seventy-five students.

Washington was known as being a malarial district. When Dr. Adams began the study of medicine any individual coming to the hospital from certain districts with indefinite symptoms, would be put down as a case of malaria. He had not found a case of malaria in five years in either of the two hospitals with which he was connected. He was told that they seldom, if ever, saw a case at the Washington barracks. The diseases seemed to run along in cycles and then entirely disappeared from the field.

So far as the case of making a diagnosis in typhoid fever was concerned, Dr. Adams agreed with most of the speakers that it was not always a difficult matter during a time of epidemic or when it resulted from house infection. The symptoms

often presented themselves in such a way that little difficulty was encountered in making a diagnosis even in the early stages of the disease. Dr. Adams had made diagnoses of typhoid fever from very meager symptoms, from the general appearance of the patients and from the histories as presented to him by the parents, which were subsequently confined.

DR. COIT asked Dr. Griffith if in his experience with reports from the laboratory there had been returned reports of a positive Widal in those cases that presented no acute manifestations of the disease. This had occurred in his experience at the Newark Babies' Hospital. This raised the question of the possibility of infants being typhoid bacilli carriers. This question of children being disseminators of typhoid fever had been carefully studied by one of the men in the employ of the United States government, and the results of his work would be presented in a paper to be read at Spring Lake, N. J., before the Medical Sociey of the State of New Jersey.

DR. GRIFFITH said that in answer to the various remarks made he would state, first, that about 60 per cent. of the infants were not over 2 years of age. The total duration of the attack in infants according to his experience was decidedly less than in later childhood, and no longer than in early childhood; which latter might be looked on as the most favorable period of life to suffer from typhoid fever. In later childhood one not infrequently finds the disease much prolonged; fever of a moderate degree continuing sometimes for weeks. In only two of the infants reported did this occur, one case having fever for thirty-six days and another for fifty-seven days. Lack of time had prevented his reading the paper in full. In the text as submitted, Dr. Churchill would find that bronchitis is referred to as of sufficient frequency to be considered a symptom rather than a complication. It was probably present in more cases than the records show. It is to be particularly noted, however, that it is seldom a symptom of any importance in infancy. The making of blood-cultures as a diagnostic test was not considered necessary. The finding of the agglutinative reaction was considered a sufficiently diagnostic symptom, and this, as his statistics show, was discovered in nearly every case examined.

As regards the leukocyte count, it must not be forgotten than this is normally decidedly higher in early life than later; 10,000 to 11,000 leukocytes per c.mm. probably being normal for early infancy. It is also to be borne in mind that hyperleukocytosis occurs in early life from many slight causes. While, therefore, a normal leukocyte count or hypoloukocytosis is strongly suggestive of typhoid fever, a hyperleukocytosis is not necessaraly a contraindication to its existence.

He again called attention to the fact that the statistics given by him did not support the statement that typhoid fever in infancy usually occurs as a house infection. In only sixteen of his seventy-five cases was there typhoid fever in other members of the family. Of course, it is perfectly possible that in some instances occurring singly there may have been typhoid carriers living in the house, but this applies with equal force to cases occurring singly in adult life, and no further consideration need be given to it here.

Finally, as to the influence of feeding, he in no way agreed with Dr. Kerley's criticism that an abandonment of milk diet would have diminished the mortality. An examination of the statistics given will show that death in a number of the fatal cases depended on complications not connected in any way with the gastro-enteric tract, and in the remaining cases there was absolutely no reason to associate the symptoms with the nature of the food given. He could claim, he thought, a rather extensive experience with typhoid fever in early life, and he had

never seen any reason to dread milk as a food in this disease. Often it was insufficient, and then the diet had to be increased by the addition of other articles. Moreover, if milk was so harmful in infancy as Dr. Kerley claimed, we should expect to see a like harmfulness shown in early childhood, but his own experience with that period, in children fed largely on milk, was that the mortality was less than at any other time of life.

As a matter of fact, a careful study of the fatal cases of the report had shown that in some of them milk was not being used at all. In other cases, which had recovered, he had observed a rapid improvement follow the change from a non-lacteous diet to one of milk. He would himself hesitate to draw any positive conclusions from these observations. Based, however, on his entire experience with typhoid fever in children, he believed thoroughly that milk was, as a rule, not a harmful food in this disease; and although he by no means neccessarily limited his patients to this when of an age to take other articles of diet, he made the increase, because, as stated, milk in itself often seemed to be insufficient and permitted too great loss of weight. This applies, however, rather to adult life and to childhood than to infancy, as the amount of milk taken in infancy is much greater in proportion to the actual body-weight than that taken in later periods of life.

SOME FUNDAMENTAL PRINCIPLES IN STUDYING INFANT METABOLISM *

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Knowledge of the energy requirements of infants and the energy content of their food is of fundamental importance in studying their rate of growth and in the treatment of nutritional disorders.

The ideal method for determining the energy transformation of infants is that of direct measurement of the heat eliminated and produced. This involves expensive, elaborate apparatus, and has been possible in but one laboratory, that of Prof. Graham Lusk in New York. Undoubtedly, the cost of this extremely accurate and delicate apparatus will preclude its ever being used extensively in hospitals.

The other method that we wish to take up is that of so-called "indirect calorimetry," i. e., a computation of the energy transformations from the gaseous exchange. It is possible to compute with considerable accuracy the energy transformations of the infant from the amount of carbon dioxid produced, and particularly from the amount of oxygen consumed. Unfortunately, direct determinations of oxygen are difficult to carry out and require complicated apparatus. The direct measurement of oxygen in young infants has been but rarely determined. The principle work has been done by Professor Lusk[1] and an associate, Dr. John Howland,[2] in the respiration calorimeter at the Cornell University Medical School in New York, and recently in the respiration apparatus of Schlossmann and Murchauser[3] in Düsseldorf.

Direct determinations of carbon dioxid produced by infants are less difficult and have frequently been made in a number of foreign laboratories. Nearly all of our knowledge of infant metabolism is based on these investigations.

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*From the Nutrition Laboratory of the Carnegie Institution of Washington.

1. Howland: Proc. Soc. Exper. Biol. and Med., 1911, viii, 63.

2. Howland: Ztschr. f. physiol. Chem., 1911, lxxiv, 1.

3. Schlossmann and Murchauser: Biochem. Ztschr., 1908, xiv, 385; xviii, 1909. 489; 1910, xxvi, 14; 1911, xxxvii, 1 and 23; Schlossmann; Deutsch. Med. Wchnschr., 1911, p. 1633.

Practically all of the researches carried out on infants in which the carbon dioxid was measured, are open to serious objections, inasmuch as there was no proper control of the muscular activity.

In all previous determinations of infant metabolism, either of direct energy transformations or by means of the direct calorimetry, either no recognition has been given to the significance of muscular movements on the part of the child, or it has been assumed that the child when not

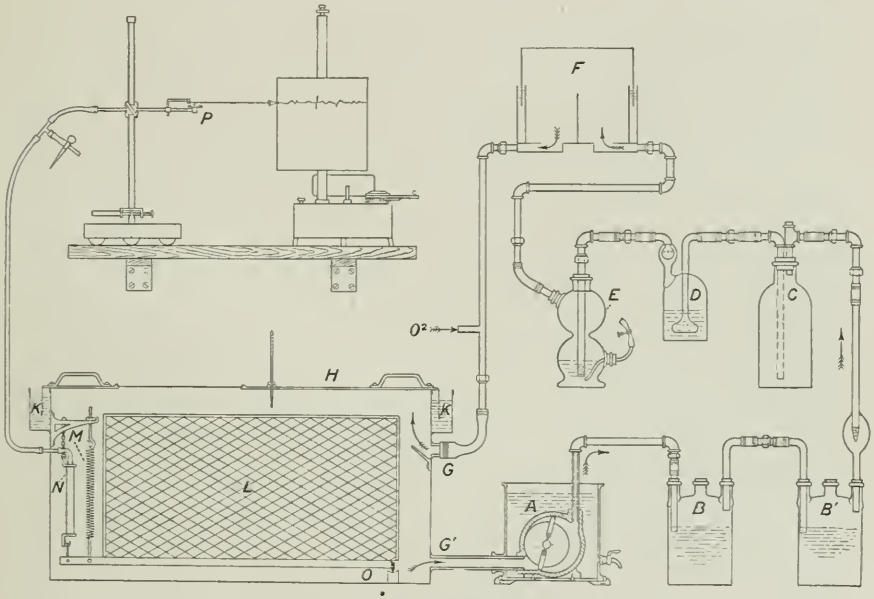

Fig. 1.—Diagram of respiration apparatus and absorbing system for determining the respiratory exchange of infants. The respiration chamber, L, in which the infant is placed is closed by a cover, H, which fits into a water seal, KK. One side of the cage, L, rests on a knife edge bearing, O, the other side being supported by a brass spring, M, fastened to a support. A tube pneumograph, N, is likewise attached to the cage, and any change in the center of gravity of the body of the infant produces an alteration in the tension of the spring, M, and the pneumograph, N. By air transmission, the tambour, P, moves a lever writing on the kymograph (the kymograph and tambour stand are drawn on a considerably enlarged scale). The air leaves the chamber at G′, enters the rotary blower, A, and then passes through sulphuric acid in two Woulff bottles B and B′. It then passes through the carbon dioxid absorber, C, and next into the drying vessel, D. Moisture is added in the vessel, E. The air then passes through a spirometer, F, which allows for contraction or expansion of air in the system and then to the respiration chamber through the opening, G. Oxygen as required is supplied through the opening O_2.

crying or obviously restless, was quiet and with constant muscular activity. In other words, the notes accompanying these reports said that the baby was either crying or quiet, i. e., asleep. The difficulties incidental to securing long experimental periods of constant muscular activity with infants are only too well known, and yet an examination of the literature shows that almost invariably all of the longer experiments on infant metabolism have included periods of obviously great muscular restlessness and activity, as well as periods of crying. While it is not necessary to show that the metabolism of an active crying infant must of necessity be considerably higher than that of a quiet child, it is not so well known that it is wholly illogical to compare the metabolism of an active, restless, normal baby with that of a quiet, sick baby, since the amount of carbon dioxid excreted depends on the degree of muscular activity.

It is our purpose in this paper to point out the inconsistencies arising from the determination of carbon dioxid in infants without taking muscular activity into consideration. We are disposed, therefore, to question the desirability of long experimental periods for establishing the basal metabolism of infants when such periods may include not only quiet sleep, but also periods of activity and even crying. It is necessary at the outset to find what is the ideal length of the experimental period in the infant. This, we consider, is the period in which the baby is asleep, absolutely quiet muscularly, and free from even the slightest tremor, and preferably without food in the stomach. And, although it is difficult to secure these ideal periods over any length of time, fortunately it can be demonstrated that if this condition exists for twenty minutes or more, a reasonably accurate measurement of the metabolism may be secured with modern perfected apparatus. The apparatus in which the experiments were made (Fig. 1) was a slight modification of that described by Benedict and Homans for experiments on hypophysectomized dogs.[4]

It was used primarily to determine the amount of carbon dioxid excreted in the air and was furnished with means of recording graphically the amount of motion of the infant. The baby was placed in a cradle or crib, *L*, one end of which was suspended on a knife edge, *O*, and the other by a stout spiral spring, *M*. Parallel to the spiral spring was a tube pneumograph, *N*, which was connected with a delicate tambour, *P*, on the outside. Any changes in position of the center of gravity of the infant produced alterations in the tension on the spring, and the pneu-

4. Benedict and Homans: Jour. Med. Research, 1912, xxv, 409.

mograph, which transmitted this change to the tambour and pointer which made a graphic record on a smoked paper drum. This pointer can be made very sensitive to motion by simple adjustment of the spring and the leverage of the tambour and, indeed, Benedict and Homans were able to obtain the respiration rate of their dogs from the record. This apparatus records the infant's slightest muscular tremors, and we were able to demonstrate that a baby could have considerable slight muscular motion, which was sufficient to affect the metabolism, and yet be imperceptible to the eye.

The babies in these researches were normal (breast-fed) babies obtained from the directory for wet nurses of the Massachusetts Babies' Hospital. The mothers of these babies were the usual type of wet nurse, all of whom had had a complete physical examination and a negative Wassermann reaction in the blood. The babies were all breast-fed with the exception of one or two who had one bottle of modified cow's milk in the twenty-four hours.

A great many determinations of carbon dioxid were made, and although the babies were awake in the morning, they did not sleep for any length of time in the afternoon, and only one or two successful periods were obtained in this manner. It was eventually necessary to work at night in a semi-darkened room where the infants kept quieter and slept for a longer time than during the day. They were all fed just before being put in the respiration chamber and consequently the results are somewhat vitiated by the specific dynamic action of the food in the stomach. In no instance were they kept in the respiration chamber when they showed any signs of discomfort. and the mothers watched the babies during the entire time that they were under observation.

It has frequently been noted in this laboratory, both with animals and with men, that there is a definite relationship between the pulse-rate and metabolism; we therefore commenced to record the pulse-rates of the infants. These were taken with a Bowles stethoscope placed over the heart of the baby, the tube of which was carried through the wall of the respiratory chamber and connected with ear pieces outside. The beat was counted for a period of one minute every three or four minutes during the entire period of the experiment. The relationship between the pulse-rate and the metabolism of the infant was found to be very close. The question then came up as to what was the minimum pulse-rate of a given age and how much and how long it could be affected by muscular exercise.

We could find no literature on this subject, and a series of investigations was, therefore, instituted by one of us (F. B. T.), in which the pulses of a number of babies were counted by a skilled nurse at the Boston Lying-In Hospital and at the Directory for Wet Nurses at the Massachusetts Babies' Hospital. The wide fluctuations found in the pulse-rate of the baby, even during periods of sleep, were astonishing, and a series of curves pointing out these pulse-rates are given herewith (Figs. 2 and 3).

The two curves given herewith are samples of a larger series and illustrate the effect of muscular exercise on the pulse taken with a Bowles stethoscope from the heart of a very young baby and that of an older baby. The most striking fact in comparing these two curves is that there is much less stability of the young babies' pulse than that of the older ones, and a slight motion causes more marked elevation of the pulse. The minimum average pulse-rate depends on the age and type of the baby, and we believe that no general rules can be made, because each baby is a law unto itself. The average of the babies in the first week of life was 120 beats per minute and that of the older babies somewhat slower. The average minimum of one three-months-old baby was about 90 beats per minute, and that of another three-months baby 100 per minute. Slight movements which were visible practically always elevated the pulse-rate 10 to 20 beats, while violent exercise, such as nursing or crying, increased the pulse-rate 50 to 60 beats. When the pulse was increased for twenty minutes, as it was during a nursing, it took about ten minutes after the exercise was finished for the pulse-rate to reach the normal. Sometimes it dropped below normal after continued exercise, and remained there for three to five minutes. The pulse, therefore, did not reach the normal line in some instances until fifteen minutes after the muscular exercise was finished.

A very close relationship was found to be established between the carbon dioxid production, the pulse-rate and the muscular movements of the infant as recorded on the smoked paper drum. In so far as possible, only those periods in which the drum indicated minimum muscular activity were used for comparison. Under these conditions the relationship between the pulse-rate and the metabolism was very apparent.

A single record will demonstrate the interesting relationships above pointed out. Record 2 with Baby 5, November 16, 1911. The baby was placed in the chamber and after some time quieted down, and the first record commenced at the point marked *I* on the curve shown herewith

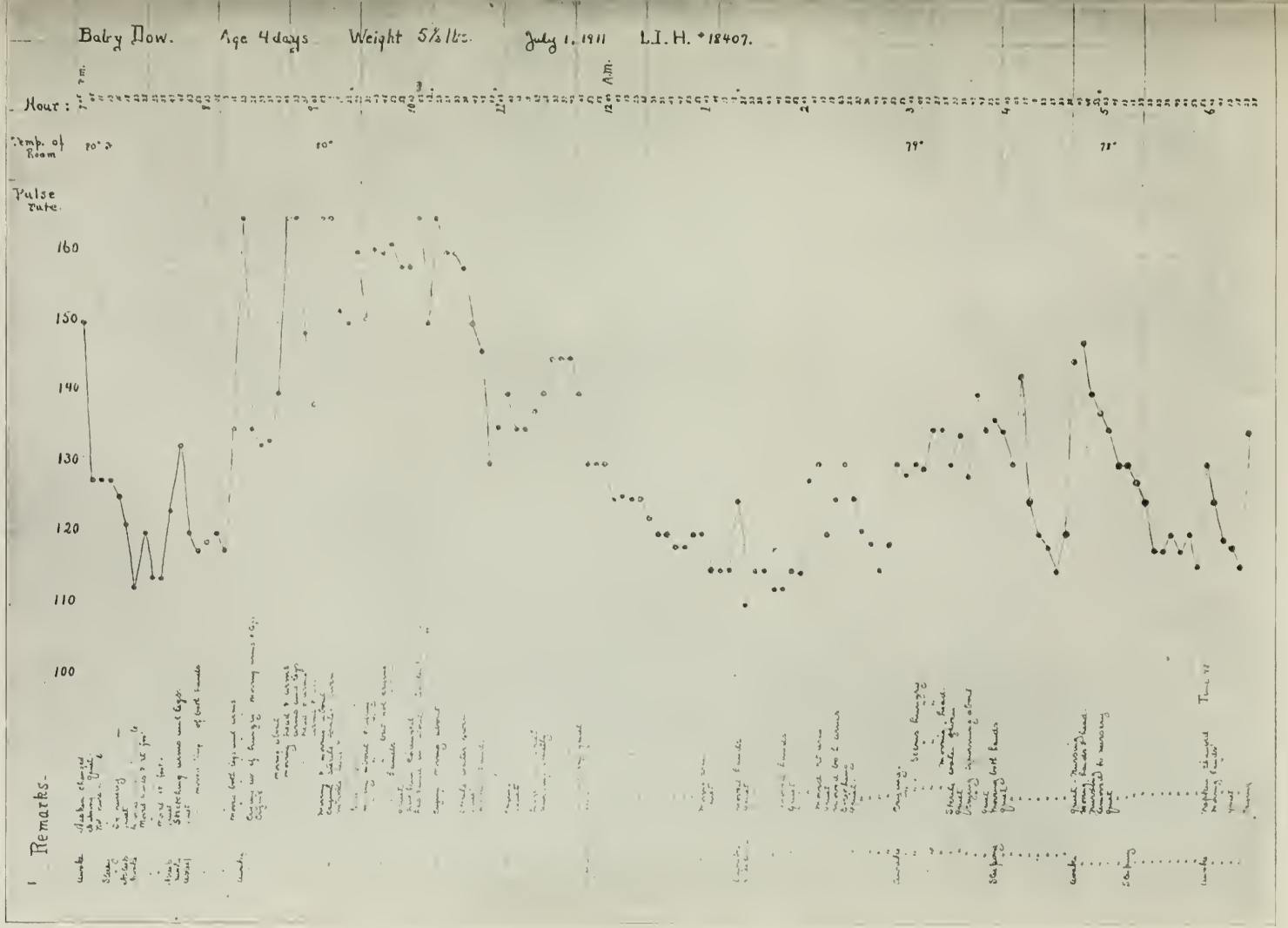

Fig. 2.—Pulse-chart of Infant Dow. Explained in the text.

(Fig. 4). The first period ended and the second began at point *II*. The results are given in the following table:

BABY 5. RECORD 2. NOVEMBER 16, 1911. WEIGHT NAKED 7.6 KILOS. AGE 7½ MONTHS

Period	Thirty Minute Periods	
	Pulse per Minute	Carbon Dioxid, Gms. per 30 Min.
1	117	3.49
2	108	2.73
3	113	2.97
4	122	3.24
5	117	3.33
6	130	3.41

Accompanying this are also given two kymograph records which show the graphic movements of the baby during the periods in which the carbon dioxid excretion was determined.

Period 1 represents the time between marks I and II on the chart. A close examination of the curve will show definite rhythmical movements which are unquestionably those of respiration. It is obvious that in Period 2, that is, from II to III, there was the minimum activity, and a comparison with the pulse-rate and carbon dioxid production shows that during this period there was the minimum pulse and the minimum carbon dioxid production. In fact, the agreement between the pulse-rate, carbon dioxid production and the graphic records on the curve is very striking. During the period from V to VI the graphic records showed a reasonably quiet period. On the other hand, during Period 5, which corresponds to this time, the carbon dioxid was slightly higher than during Period 4. This undoubtedly can be explained by the fact that the greatest activity during Period 4 was just before the end of the period, and unquestionably there was an accumulation of carbon dioxid in the chamber which was not swept out before Period 5 began. At this time residual analyses of the air in the chamber were not made, as it was found that the ventilation was sufficiently rapid to maintain the carbon dioxid content of the air at approximately .06 per cent. throughout the whole test. For extreme accuracy, it is obvious, therefore, that there should be a determination of the carbon dioxid at the end of each individual period. The excessive activity at the end of Period 6 was caused by the child's waking up and the last few minutes crying lustily.

While to the eye the child was "quiet" throughout all but the last period and apparently "absolutely quiet" in both Periods 2 and 3, the

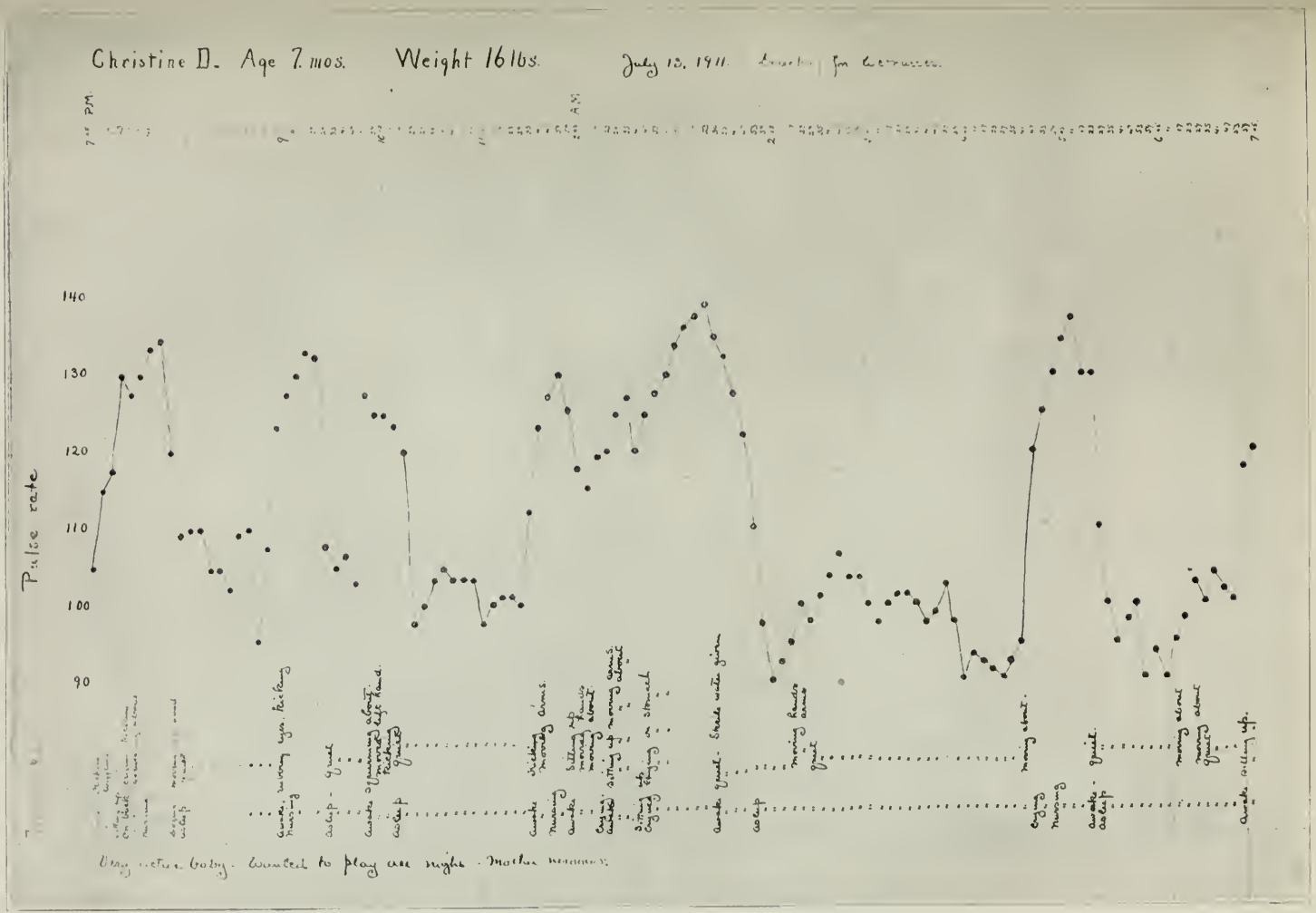

Fig. 3.—Pulse-chart in Infant Christine D. Explained in the text.

graphic records show considerably greater muscular activity during Period 3 than in Period 2, and enough to produce almost a 10 per cent. increase in the metabolism.

Although the results of our investigations on the whole are not yet ready for publication, we feel convinced of the importance of considering in all subsequent metabolism experiments the pulse-rate of the infant, and particularly the degree of muscular activity. The enormous variations in the total metabolism as affected by what might otherwise appear to be slight muscular activity, are such as to lead us to question seriously all experiments made in twenty-four periods, and we wish to assert that all metabolism experiments on infants made without known controlled pulse-rates and without graphic records of muscular activity are lessened enormously in value by the absence of these important factors.

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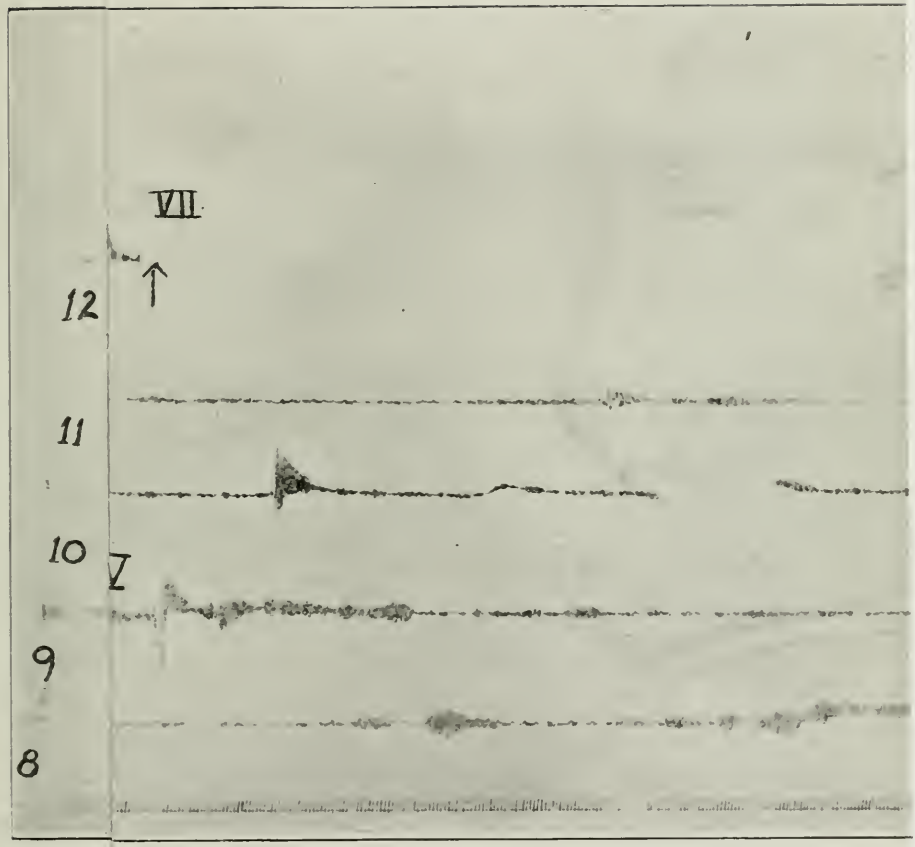
DISCUSSION

DR. HOWLAND said that the work of Drs. Talbot and Benedict was very valuable and that if it were possible to further improve the apparatus with which the results had been obtained, so that the amount of oxygen could be determined as well as the amount of carbon dioxid, it would add enormously to our facilities. Apparatus such as that used by Dr. Graham Lusk of New York for determining directly the radiation of heat as well as the amount of oxygen consumed and the carbon dioxid eliminated, while perfectly accurate, was altogether too elaborate and costly for general use. The methods employed in this country for the determination of the respiratory exchange differed widely from those employed abroad and it was therefore very difficult to arrive at a satisfactory basis for the comparison of results. The periods in the European experiments were usually long, often twenty hours in length, the children being asleep or awake and often crying. By this method it was hoped to reach an average for the whole day. The American experiments were made only during periods of absolutely quiet sleep and were not more than one-half to three hours in length, on the theory that only between periods of absolute quiet were comparisons possible. It was therefore difficult to compare results obtained in two entirely different ways.

Dr. Howland asked Dr. Talbot if a perfecting of the apparatus was possible, so that the amount of oxygen consumed could with accuracy be measured.

DR. HAMILL asked Dr. Talbot whether there was a definite relation between the heart rate and the muscular activity.

DR. TALBOT closing the discussion said that there is a definite relation between pulse rate and muscular activity, which is shown only in degree and not by absolute figures. During the greatest muscular activity the pulse went to its highest point and sometimes increased 50 to 60 beats per minute. He did not have, however, sufficient figures to enable him to draw any conclusions as to how much the elevation of the pulse would modify the amount of carbon dioxid excreted. He could only state that there was a definite relationship between the pulse rate and the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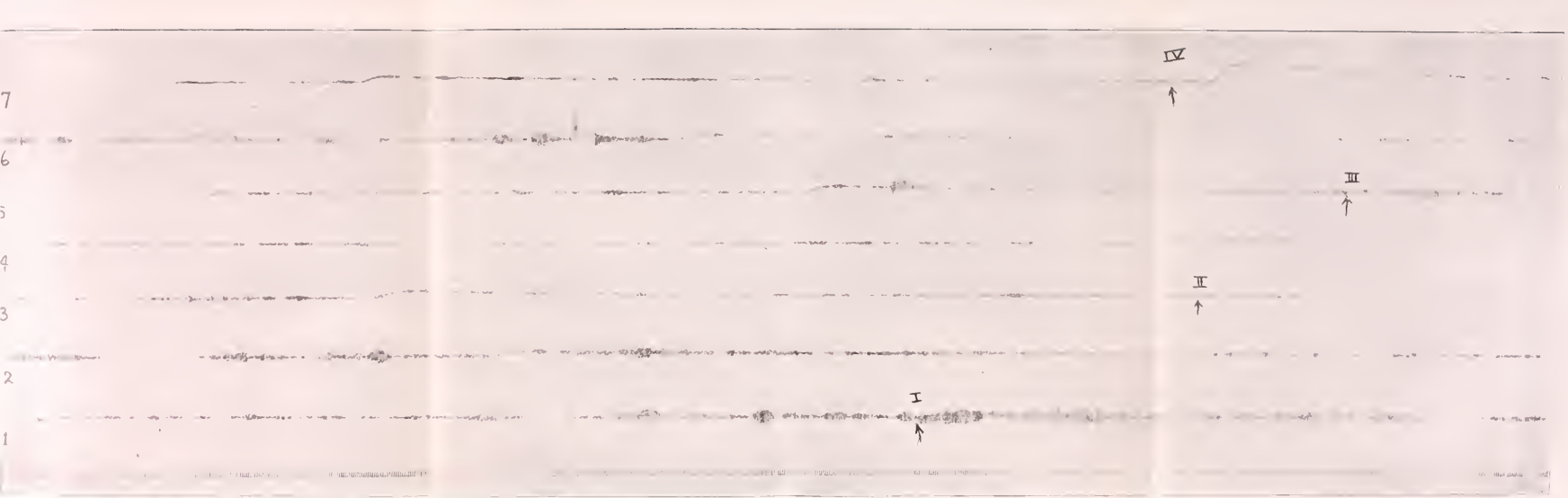
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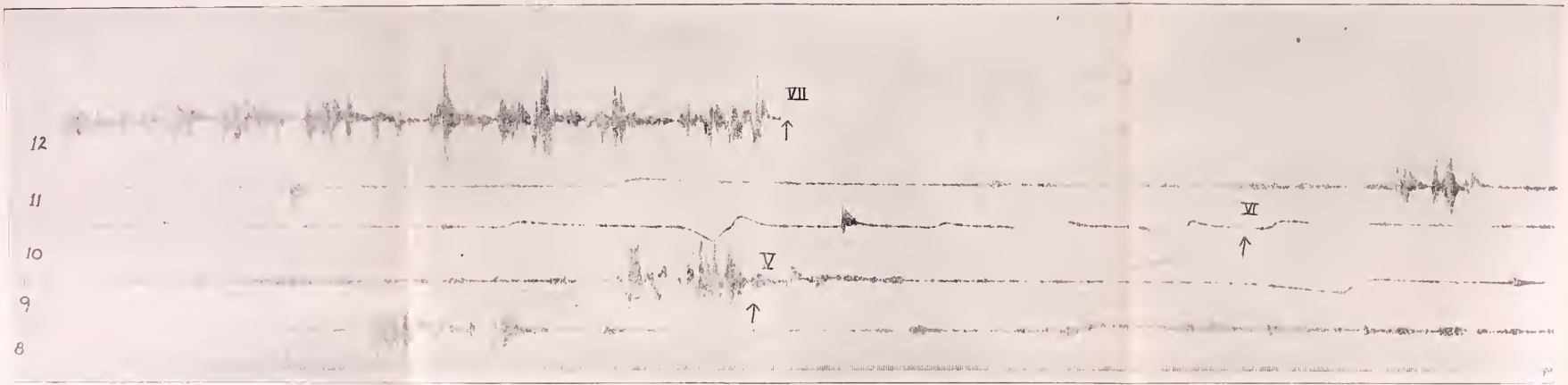
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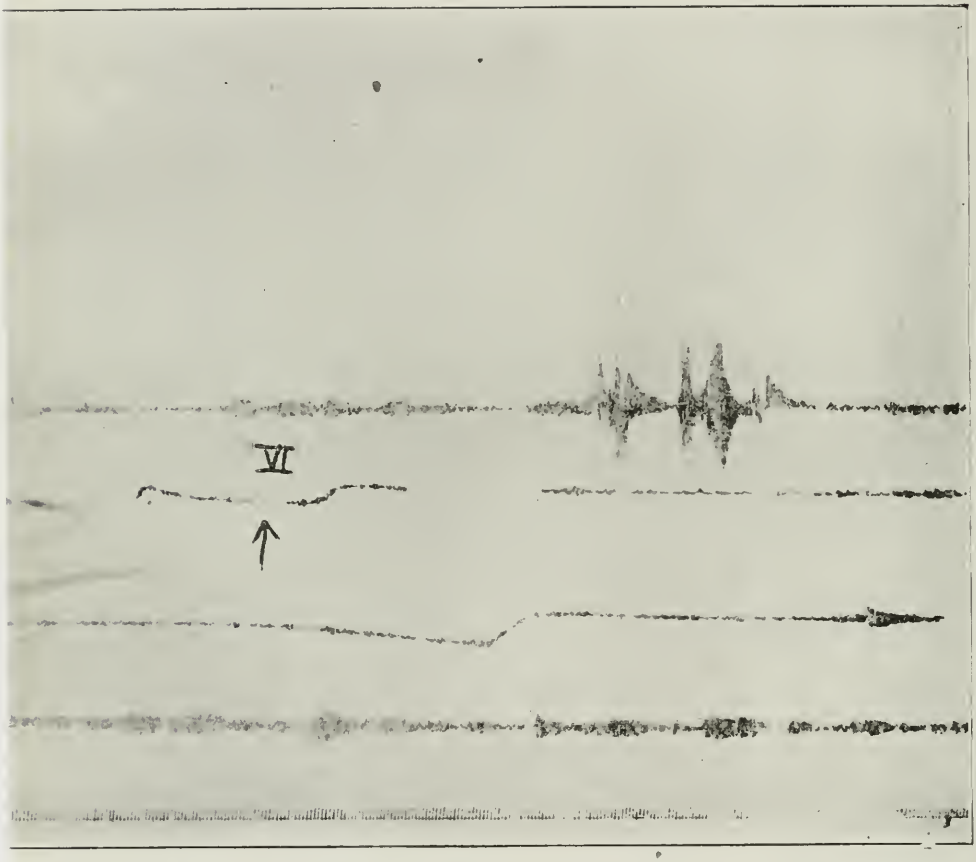
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amount of carbon dioxid excreted. In the charts he passed around it was shown that the pulse rate increased with the amount of muscular exercise. If the charts were sufficiently studied it would be noticed that, in certaion instances, there was not sufficient exercise recorded to correspond to the elevation of the pulse rate. His only explanation for this was that the pulse rate was only taken once in every six minutes and the baby might have moved two minutes before the pulse was taken. With regard to the determination of the amount of oxygen, he hoped that by next fall they would so perfect their apparatus that this would be possible.

A CASE OF DELAYED DEVELOPMENT IN A BOY TREATED WITH THYMUS GLAND

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The physiology of the thymus gland is very imperfectly understood. No one of the ductless glands appears to have a more active part in the economy, especially in the younger years of life, and yet its complete removal is not accompanied by those striking manifestations which follow removal of the thyroid or adrenal. It cannot be concluded, however, that because the removal of a gland is not followed by an acute death, it plays no important part in nutrition. The evidence afforded by removal of the sexual glands is proof on this point.

The laboratory investigations are not altogether in accord. Certain points, however, seem to be fairly well established. The thymus remains in an active condition during the presexual life of an animal, but with the onset of sexual maturity it undergoes a retrogression which finally amounts to an almost complete atrophy. The involution of the thymus appears to be a more rapid process when the sexual glands become mature. When castration is performed before puberty the thymus does not show the same degree of involution found in normal animals. Some observations point to the belief that thymectomy in guinea-pigs is followed by an earlier ripening of the sexual glands, while other experiments with chickens show that thymectomized birds have much smaller sexual glands than the controls. There appears to be an intimate relation between thymus and sex glands in respect to their mutual development and also with respect to the effect on nutrition.

The second point in which there seems to be some agreement in the experiments is in the relation of thymus removal to the development of the skeleton. While thymectomy is not followed by an acute death, the animals subjected to the operation do not in many cases grow to the same size, have the strength, or show the resistance to infection exhibited by controls. In respect to the bones, they are of a smaller size, are softer,

and the epiphyseal line is broader and more irregular compared with controls.

These conclusions seem to have a fairly definite relation to the results obtained in the treatment of the case about to be described.

There has been no active substance found in the thymus which compares with adrenalin or iodothyrin. For therapeutic purposes the whole gland, either fresh or dried, has been administered in most instances. Until thymus implantation is perfected or until the active principle is discovered, such a method seems the only one available.

In February, 1910, a mother referred by Dr. Brooks Wells brought her son, aged 16 years and 4 months, to consult one of us (Kerley) regarding what she termed "a failure of development." She stated that the boy had made no perceptible growth in over two years, that his genitals were small and undeveloped, and that the testicles were not in the scrotum. She was greatly worried, fearing that the boy would never be a man. Her statement further was to the effect that the boy was mentally sound, was active in play, and normal in mentality, as proved by his standing in school. He was in classes corresponding to other boys of his age.

Examination showed the boy to be delicate in appearance, normal in all respects excepting that he was undersized, his height being 56 inches and his weight 76 pounds stripped, both weight and height being about that of a boy, aged 11 to 12 years.

The penis was small and shrunken, the testicles were very small, and although there was no retention and they could readily be brought into the scrotum, they rested in the canal a greater part of the time. There had never been an erection of the penis, and there was neither pubic hair nor hair in the axilla.

The treatment instituted was that of lightening the school work, more hours in bed, and a suitable diet. Tincture nucis vomici, arsenic, and cod-liver oil comprised the medication. The patient was seen at about one month intervals during the following nine months. At this time there was a gain of 3 pounds in weight. His height was the same and there was no change whatsoever in the sexual development. The family were extremely troubled and requested that every effort be used in the boy's interest. At the suggestion of Dr. Beebe, all medication was discontinued and desiccated thymus extract, 15 grains daily, was prescribed.

During the first six months of thymus administration the genitals, penis, and testicles perceptibly enlarged, and after nine months' use the first erection occurred when aged 17 years and 10 months. This was new and novel and amused the patient very much. At the completion of one year treatment, when aged 18 years, hair appeared on the pubis and in the axilla. He had gained 1 inch during the year, standing 57 inches, and had gained 11 pounds, weighing 87 pounds.

During the next six months, which brings us to April of this year, 1912, when aged 18 years and 6 months, he had gained 2 inches in height, bringing him at the present time to 59 inches in height, and gained 8¼ pounds in weight, increasing the weight to 95¼ pounds. The testicles have remained in the scrotum during the last six months. The voice changed in February of this year, when he was aged 18 years and 4 months.

In the eighteen months under treatment there was a gain of 3 inches in height after he was aged 17 years, and 19¼ pounds in weight when there had been no growth according to the mother's statement for two years and nine months before.

The sexual organs are apparently normal and well developed. The use of the thymus might be considered a coincident in a case of retarded development; such cases of late development, however, are most unusual. No claims are made for the thymus. We appreciate that one case proves but little.

Six other cases of slow growth or retarded development are under observation with thymus at the present time. These cases will be reported later and will help to establish the point that naturally will arise in the mind of the reader whether or no thymus was operative in the case reported or whether it is to be looked on as a coincident, and that the phenomena we observed would have taken place without its use.

DISCUSSION

DR. HOLT said the report was most interesting but not quite conclusive. He had seen many boys who had developed very slowly for a long time take a start and improve remarkably and without any specific medication or in fact any obvious reason. He had seen backward boys who had been sent to a ranch out West make most surprising growth. One should be very careful in drawing conclusions regarding results of specific remedies. Dr. Holt heartily endorsed what was said in the paper regarding the rest treatment for children who were not thriving.

DR. RUHRÄH referred to the use of thymus extract in marantic babies; in many cases of advanced marasmus he had used it and the results obtained were about the same as those when the thymus was not used. There occurred about

the same percentage of improvements. However, he always felt that there was some close relation between growth and the thymus, and that if it were possible to give enough, or by some other method, one might obtain very satisfactory results from its use. In connection with thymus extract medication in cases of malnutrition, it was interesting to note that Williams had obtained wonderfully striking results in these cases from the use of thyroid and Dr. Ruhräh tried to find out what cases the thyroid benefited and he found that it was a case of "hit and miss." A very few cases were benefited but he could not tell before hand which ones would be and which ones would not.

DR. HOWLAND said that so far as experimental evidence went it was possible to get evidence of almost any kind in regard to the thymus. A great many experimentors had enucleated the thymus in animals but without any very definite results. There was also considerable number of children from whom the thymus had been removed on account of tracheal stenosis and no published statements had appeared as to permanent injury or lack of development as a result of the removal of the thymus. Any medication such as this was like hitting in the dark; any other gland might have been used with as good reason and probably with a similar result.

DR. CHURCHILL said that he could not agree with what Dr. Howland had stated. There were only forty-five or fifty cases on record but they had not been followed a sufficient length of time, e. g., up to puberty, to warrant drawing conclusions. It was impossible to remove entirely the thymus gland in infants; no matter how small the gland may be, after the completion of the operation there will be enough left behind to carry on its function.

DR. GRIFFITH said that Dr. Kerley's paper was certainly suggestive, but that he felt that as yet our knowledge of the action of the various internal secretions was too limited, in most conditions at least, to allow us to reach any certain conclusions regarding their influence on growth. A few years ago a Belgian physician extolled the effects of thyroid extract in overcoming stunted growth. Dr. Griffith had tried this, but without result in cases of cretinism. Many of the other glands had been recommended, among them more recently the pituitary body; and he had tried this also, but with no definite effect. As regards the thymus gland in particular, he shared the opinion of others that its atrophy or imperfect action is rather the result of the general malnutrition than the cause of this. In the general treatment of children of delicate constitution, with insufficient bodily development, we may well take lessons from the neurologists in their application of the rest cure. No child knows how to take care of himself, nor do the parents know how to care for him. The child does not know, nor is he told, when to stop playing or working. The result is an overdoing of exercise. Parents, as a rule, push their children mentally and physically too greatly. For a number of years Dr. Griffith had laid great stress on systematic rest of the child for some portion of the daylight hours, and he had been convinced that the results were good.

Dr Heiman thought that the treatment by these organic products was empirical; he would state, however, that in a great many of these cases of stunted growth in infants, the administration of thyroid in one-tenth grain doses three times a week gave excellent results. Dr. Kerley's case appeared to be one of infantilism.

DR. KERLEY said that so long as they could keep the little fellow growing they would continue the use of this agent. The paper was to looked on as an exhibit and they did not attempt to draw conclusions. He had other cases under observation and these would be reported later.

THE DEXTRINS AND MALTOSE IN INFANT FEEDING

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During the progress of pediatric research into the physiologic relations to the organism of the various elements of an infant's food, attention has recently converged upon the part played by the carbohydrates, both as destructive and constructive agencies. The importance of carbohydrates in furnishing to the normal body fuel for energy and heat requires no recapitulation. It is rather the injurious effects on the human body of carbohydrate intolerance, and, during recovery from such conditions, the relative toleration and absorbability of the different saccharids that has most keenly gripped our attention.

In health, the infant has seemed to take with about equal facility the three sugars most commonly employed in making up the deficiency of carbohydrates in diluted cow's milk—namely, milk sugar, cane sugar, and so-called malt sugar—but it has remained for recent investigations of the pathology of nutrition to assign to each of these forms of sugar its relative position as a disturbing factor. Following the dictum that nothing should enter into the composition of an infant's food which did not appear in breast milk, it would have been natural to suppose that cane sugar and malt sugar, as extraneous substances, would be found to be the more deleterious. On the contrary, recent investigations have placed the chief stigma on the lactose of cow's milk, even though present as a natural constituent of such milk.

In now rearranging the sugars in the order in which they are best borne after injury by the carbohydrates—namely, as malt sugar, cane sugar, and milk sugar—we seem to have overlooked previously the fact that so-called malt sugar has always been a common source of human nutriment when formed from the starchy elements of the diet by the activities of the digestive ferments. Although the advantages of the so-called malt sugar, or maltose, have recently again received wide recognition for purposes of restoring deficient or halting nutrition in infants, and for furnishing sufficient calories during recovery from food injuries, there has been little appreciation of the rationale of its action.

At the outset of such an inquiry, it must be grasped that the terms malt sugar and maltose, as applied to the substances commonly employed in infant feeding, are inaccurate and misleading. While pure maltose in the strictly chemical sense is a rare product of the laboratory, too expensive for general use and consequently never employed in infant feeding, the commercial products to which this generic name is too often loosely applied, are numerous and it is doubtful whether any two of them have exactly the same composition. The term embraces almost any preparation produced by the action of diastasic ferments on starch, but the result of such action by well-known chemical laws is never in practice pure maltose. Making all allowance for the divergencies of experimental authorities, and independent of whether the active enzyme be the diastase of germinating grain or the animal enzymes, ptyalin or amylopsin, the result of such action on starch is a mixture of the various dextrins with maltose. The composition of the resulting admixture is not a negligible one, as will be seen if we trace the various steps of its formation from raw starch.

The grains of raw starch, a polysaccharid, give a blue color when tested with iodin. When boiled, they swell, rupturing the cellulose envelope, taking up water in physical combination and forming a jelly. A small portion of this gelatinized starch, which is soluble in water and known as amylodextrin, also gives with iodin the blue reaction of starch. The addition, however, to the mass of gelatinized starch of a small amount of one of the diastasic enzymes suffices to bring the water into chemical combination with the starch, the blue color is no longer evoked by iodin, and as the action of the enzyme progresses there is produced, together with maltose, an important group of dextrins. These dextrins, probably of different molecular weights, are, as is well known, erythrodextrin, giving a red color with iodin; achroodextrin, which is colorless, with iodin; and, finally, maltodextrin. Other intermediate stages have also been described.

Whether maltose is successively split off from the starch with each advancing step of the dextrin chain, or is the final product of that chain, is disputed. It suffices for our purpose that after the addition of the enzyme to the starch, both maltose and dextrins are present, whose proportions vary markedly with the conditions under which the transformation has taken place; and that pure maltose is never produced, because the presence of sufficient maltose inhibits the further evolution of the dextrins until the excess of maltose is removed.

We have, then, in the same mixture, maltose, which is a disaccharid and crystalloid, fermentable and dialyzable, and dextrins, which are polysaccharids, reversible protective colloids, non-fermentable and non-dialyzable. Surely such contrasting properties must have attracted the attention of those who employed them largely in infant feeding. We turn, however, in vain to much of the most important literature on the practical use of malt preparations for such mention. In it we find surprisingly little interest in the dextrins. Many authors are still content to speak of maltose as though it were alone worthy of mention.

One is therefore forced to the conclusion that while the demands of science led to a subconscious formal recognition of the presence of dextrins, they were long treated in pediatric literature as negligible though unavoidable accompaniments of maltose, to the presence of which latter sugar in the various malt products was ascribed whatever virtue the combination might possess.

There is nothing essentially new in the use of maltose and dextrin in the human economy. It is as old as the digestion of starch. It was rendered practicable for infant feeding by von Liebig, and has survived in various forms since his death. Chapin employed it in dextrinizing gruels: Keller gave it a new impetus abroad in his malt-soup; and it is now considered by Finkelstein essential to the reclamation of the infant suffering from "dyspepsia, decomposition, and intoxication." It is but natural that while accepting the clinical testimony we should inquire why it should be so valuable, and to what properties it owes its present-day popularity. A perusal of the literature would indicate that its use has been urged chiefly because it is less fermentable and because more of it can be absorbed than of other sugars, such properties being ascribed usually to its component maltose. Let us see whether some clear statements can be formulated which will be of service to the student of infant nutrition.

The carbohydrates, as a group, are carbon carriers furnishing fuel to the body for combustion by oxidation. The choice between them lies, then, chiefly in their suitability to the individual and the ease with which they are converted and absorbed without untoward by-effects. Clinical experience has fully demonstrated that either lactose, saccharose, or maltosedextrins could be used successfully in feeding innumerable normal infants. The question of choice between them arises chiefly when disturbances of digestion occur during the administration of any one of the three. Starch, also, in moderate quantities, has been so largely

employed in the food of infants that there is no longer any question of its utilization by the organism when transformed, of course, by the digestive processes into dextrin and maltose.

The accompanying table arranges the commonly employed carbohydrates with reference to their supposed molecular complexity, their chemical relations, and their properties. Attention should be directed to the fact that both starch and the dextrins are polysaccharids, while the end products into which the latter are finally split by the enzymes during digestion are monosaccharids. But while polysaccharids and disaccharids enter as such into some of the many mixtures used for infant feeding, these must be reduced to monosaccharids for normal absorption. Dextrose is recognized as the most suitable monosaccharid for this purpose, since galactose and levulose must undergo a further process of inversion to dextrose. It therefore would appear that maltose, which splits into two molecules of dextrose, may be absorbed with less labor than either lactose or saccharose.

MILK-SUGAR	CANE-SUGAR	MALT-SUGAR		
		Starch (amylum)	Polysaccharides	Colloids (reversible, protective) Non-fermentable Non-dialyzable
		Amylodextrin Erythrodextrin Achroodextrin Maltodextrin		
Lactose	Saccharose	Maltose	Disaccharides	Crystaloids Fermentable Dialyzable
Dextrose + galactose	Dextrose + levulose	Dextrose + dextrose	Monosaccharides	

Nevertheless, while lactose and saccharose are given in the food by themselves, maltose is never administered without an admixture of dextrins, which latter, while capable of being further elaborated into maltose, and subsequently into dextrose, have, for the time being, very different chemical and physical properties. This association, then, of the dextrins with maltose, instead of being a negligible matter, is a factor of considerable importance and may be assumed to play a large part in the favorable effects of the malt preparations in disturbed conditions.

It is now recognized that the ingestion at one time of large quantities of one of the sugars may produce diarrhea, and that this diarrhea results from irritation of the small intestine, either by the sugar itself or by the products of its fermentation. This increases peristalsis and hurries the

contents through the intestine, allowing insufficient opportunity for proper elaboration and absorption. The irritation may, moreover, be sufficient to cause injury to the mucous membrane and exfoliation of its important epithelium. Now, the polysaccharid starch, if gelatinized, when combined with sugar, which would, if given alone, cause irritation of the intestine, is apparently capable of acting as a protection to the mucous membrane, either by preventing rapid absorption of the sugar or by a mechanical action similar to that of the familiar starch enema upon the lower bowel. Keller was forced to make use of this protective property of starch to enable him to employ larger quantities of his malt-soup extract than would otherwise be tolerated without disturbance.

Thin barley gruels, when substituted for a plain water diluent, have been found to be particularly helpful where disturbance of intestinal digestion has arisen during the use of milk and lactose or of milk and saccharose mixtures. It is therefore worth considering whether the advantages of barley gruel are due wholly to its effect on the protein curd, and not also, in part at least, to this same protective property of gelatinized starch. Furthermore, we may find in the same principle an explanation of the empirical but successful use of cereal decoctions in the early stages of summer diarrhea, quite apart from the restraining effect of carbohydrates on putrefactive bacteria and the known value of a carbohydrate diet in favoring a retention of fluids in the body tissues.

Such being the action of gelatinized starch, it is reasonable to assume that dextrin subserves a similar function, since it is also a polysaccharid and closely related to gelatinized starch in its clinical and physical properties. This protective action of the dextrin is not, however, the sole advantage of the maltosedextrin combination over the pure disaccharid sugars. The maltosedextrin mixture, when given in equal or even in somewhat greater amounts than lactose or saccharose, offers for immediate absorption only a portion of its potential sugar. On the one hand, the moderate quantity of immediately available maltose does not so readily overtax the absorptive mechanism nor overwhelm the intestine or the organism with a flood of sugar; while, on the other hand, the reserve sugar in the form of dextrin, being non-dialyzable, does not readily pass through the intestinal wall but may be gradually transformed into maltose and absorbed as it is needed during the undisturbed progress of the chyme through the bowel. It is entirely conceivable that an excess of sugar in the intestine might easily prove too much for the orderly processes of the splitting enzymes, and lead to the absorption of

unchanged sugar, which would throw a secondary strain on the entire organism.

If, however, we accept the more modern view that while all carbohydrates are normally transformed into dextrose before absorption and stored in the liver as glycogen, all the sugar normally leaving that organ in the blood is in the form of maltose, the direct absorption of maltose from the gastro-intestinal tract becomes a matter of much less serious moment than a similar absorption of unchanged lactose or saccharose. In fact, it seems exceedingly probable that one of the chief reasons for the prompt improvement often seen in the condition and the weight of exhausted marasmic infants when a malt-sugar preparation is substituted for one of the other sugars, is because some of the maltose is absorbed as such and furnishes an immediately available fund of energy for the not inconsiderable labor of digesting the rest of the meal.

Although malt preparations are spoken of as less fermentable than the other sugars, it is, of course, an error to think of maltose itself as not liable to fermentation of certain types, since this property of maltose is relied on in all brewing operations. Nevertheless, the cleavage of maltose into two quickly absorbable molecules of dextrose may proceed so readily that less opportunity is afforded for attack by undesirable ferments. Dextrin, on the contrary, which remains unfermented in beer, is immune to fermentation in the intestine until reduced to assimilable maltose, and in this manner the clinical experience with the maltosedextrin combination is readily explained.

Having demonstrated that the presence of dextrins plays no small part in the therapeutic and nutritive values of maltosedextrin preparations, our attention is directed to the proportion in which these are present in the commercial products:

	Maltose	Dextrin
	%	%
Soxhlet's Nahrzucker	52.44	41.21
Loeflund's Nahrmaltose	40.00	60.00
Dextrimaltose (Mead-Johnson)	51.00	47.00
Neutral maltose (Maltzyme Co.)	63.–66.	8.–9.
Loeflund's malt-soup extract	58.91	15.42
Borcherdt's malt-soup extract	57.57	15.76

It will be noted that the dry preparations contain 40 to 60 per cent. of dextrin and that the semi-fluid preparations contain 10 to 15 per cent.

The latter, however, in making malt soup are combined with gelatinized starch.

That the proportions vary is not surprising when one considers that the concentration and reaction of the solution, the temperature at which conversion takes place, and the length of time that the enzyme is allowed to act on the grain or starch markedly influence the extent of the conversion into maltose and dextrin and determine which of the two shall preponderate.

Thus far, we have been accustomed to rely on the clinical results obtainable by the use of one or other of the stereotyped commerical preparations of more or less fixed proportions. An exceedingly interesting field of research is now open for determining the nutritive and therapeutic values in normal and pathologic cases of high, average or low percentages of dextrin in maltose-dextrin mixtures. This would present no great difficulties, since temperatures below 55 C. (131 F.) produce the largest amount of maltose, and above 63 C. (145 F.) produce the dextrins in excess, until a temperature of 75 C. (167 F.) stops the action of the enzymes. There would, indeed, seem to be little excuse for always using the same proportions of maltose and dextrin, and a reasonable expectation that more favorable results might be obtained in selected cases by varying the proportions as we are wont to do with other constituents of the infant's food having diverse properties.

However, both milk and cane sugar have proved, in our hands, eminently satisfactory in so many normal cases that we need not feel called on to yield hysterically to the temptation to employ the more expensive malt products exclusively, yet any knowledge which we may acquire of the behavior of the different carbohydrates places their use on a more scientific basis and must inevitably increase our resources for meeting promptly and efficiently deviations from normal digestive conditions.

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MALTOSE IN INFANT FEEDING

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Three different sugars are used commonly in the feeding of infants, lactose, saccharose, and maltose. Maltose is seldom, if ever, used in the pure form. Almost all of the sugars which are spoken of as malt sugars are in reality combinations of maltose and dextrin, for example: Soxhlet's Nährzucker equals maltose 52.44 per cent., dextrin 41.26 per cent.; Löflund's Nährzucker equals maltose 40 per cent., dextrin 60 per cent.; Mead's Dextri-Maltose equals maltose 51 per cent., dextrin 47 per cent.; Maltose of Walker-Gordon Laboratory equals maltose 57.1 per cent., dextrin 30.9 per cent.; Mellin's Food equals maltose 60.8 per cent., dextrin 19.2 per cent.

These sugars are all disaccharids, lactose being a combination of dextrose and galactose, saccharose of dextrose and levulose, and maltose of dextrose and dextrose. The dextrins are bodies which are formed in the change from starch to maltose. There are a great variety of them and their exact composition is not well known. The dextrins being finally converted to maltose, their ultimate end is dextrose.

The disaccharids are not absorbed as such from the intestine under normal conditions, but are first broken down into their respective monosaccharids by special ferments. These ferments are maltase, saccharase (invertin) and lactase. They are formed in the mucous membrane of the small intestine. Lactase is more abundant in the upper than in the lower portion of the small intestine. Maltase is also present in the blood, the saliva and the pancreatic juice. Saccharase is present in the intestinal mucous membrane at the beginning of the fourth month of fetal life and maltase at the end of the fourth month. Lactase appears in the seventh or eighth month. Lactase is usually the least abundant at birth, but soon increases when milk is given.

The monosaccharids which are formed are taken up by the portal capillaries and carried by the portal vein to the liver where they are converted into and stored as glycogen, to be later reconverted by the maltase in the blood into dextrose and used as required.

If an excessive amount of a disaccharid is introduced into the intestine, or there is a lesion of the intestinal wall, it will pass into the circulation before it is broken down into the monosaccharids. When the disaccharids reach the circulation in this way or are introduced directly into the circulation, all the lactose and the major part of the saccharose are eliminated unchanged in the urine, there being no ferment in the blood which is capable of breaking down these sugars. The rest of the saccharose is eliminated through the gastric mucosa, the salivary glands, and in the bile. The maltose is, on the other hand, broken down by the maltose in the blood, and unless in great excess, is retained. The limits of assimilation of the disaccharids in infancy are: Lactose, 3.1 to 3.6 grams per kilogram; saccharose, no data, probably about the same as lactose; maltose, 7.7 grams per kilogram.

Maltose is the most quickly absorbed of the three disaccharids, saccharose next, and lactose much less rapidly. On the other hand, however, when equal amounts of these sugars are given, considerably more malt sugar is excreted in the feces than milk sugar (Hartje). In fact, under normal conditions lactose is never found in the feces (Péhu and Porcher) unless the food contains more than 7 per cent. of milk sugar (Hartje).

When the disaccharids are added to a food which contains little or no sugar there is a rapid increase in weight, owing to the lessened elimination of water by the kidneys as the result of the presence in the organism of the products of the assimilation of the sugar absorbed. The gain in weight is more rapid with maltose and saccharose than with lactose, probably because of the more rapid absorption of these sugars.

Finkelstein believes that sugar may cause fever, and in his papers has devoted much attention to the so-called "sugar fevers." Leopold found that 43 per cent. of the babies tested with lactose, 42 per cent. of those with saccharose, and 33 per cent. of those with maltose reacted with fever. This fever was, however, always accompanied by diarrhea, and in none of the cases tested in which the stools remained normal did the sugar cause fever. Schlutz's recent experiments make it appear very improbable, moreover, that, even when there are lesions of the intestine, the rise in temperature is caused directly by the sugar.

The disaccharids are all fermentable. Lactose undergoes lactic acid fermentation more readily than the other sugars. Saccharose undergoes alcoholic fermentation most easily and butyric acid fermentation next most readily, while maltose is especially prone to butyric fermentation and next to alcoholic.

It is generally accepted that under normal conditions, and when not given in excess, lactose and maltose have a slightly laxative and saccharose a slightly constipating action. Leopold has recently found that when lactose, saccharose, maltose and dextrin-maltose mixtures are given to normal or almost normal infants by mouth in equal amounts, the dextrin-maltose mixtures produce diarrhea less easily than the pure disaccharids and that lactose causes diarrhea more easily than either of the other sugars. Sixty-six per cent. of the babies which were given lactose, 21 per cent. of those given saccharose, 16 per cent. of those which received maltose, and only 5 per cent. of those which took the dextrin-maltose mixtures developed diarrhea. The probable explanation of the greater frequency with which lactose caused diarrhea is its relatively slow absorbability.

It has been claimed that the lactose of cows' milk is not identical with that of human milk. There is, however, no convincing evidence in favor of this claim. No differences having thus far been found in the chemical composition of lactose from different sources, it seems more reasonable, therefore, to consider them identical until they are proved not to be.

The normal fecal flora of the breast-fed infant, according to Kendall, is comprised of the following organisms: *Bacillus bifidus, Micrococcus ovalis, Bacillus coli, Bacterium aërogenes* and *Bacillus acidophilus. Bacterium aërogenes* appears in the upper levels of the tract, the duodenum and jejunum; *Micrococcus ovalis* in the lower jejunum, the ileum, and to the ileocecal valve; *Bacillus coli* and *Bacillus acidophilus* in the region of the ilecocecal value, while the *Bacillus bifidus* appears to dominate the ascending and transverse colon. The composition and maintenance of the normal fecal flora is without question due to the relative excess of carbohydrate, in the form of lactose, in the milk. Microscopically with the Gram stain, when babies are fed on cows' milk, there is a relative increase in Gram-negative bacilli of the colon-aërogenes type and of coccal forms of the *Micrococcus ovalis* type, associated with the diminution of the bifidus type. Three butyric acid-forming organisms have been isolated by Passini from the stools of apparently normal bottle-fed babies. These are all anaërobes, and one of them, Bacillus perfringens (Bacterium Welchii) is a cause of a not uncommon type of infantile diarrhea. This organism has also been found by Sittler and many other observers.

It is, therefore, of great importance, in order to maintain the normal fecal flora, to have a considerable amount of sugar in the food of babies

fed on mixtures of cows' milk. According to Kendall, lactose favors especially the development of *Bacillus bifidus,* which is normally the predominant organism in the large intestine, while maltose is especially conducive to the growth of the *Bacillus acidophilus,* which, although normally present in small numbers, if present in large numbers is liable to produce an excessive degree of acidity which may cause irritation of the intestine and an intolerance for sugar. Under normal conditions, therefore, as far as regards the maintenance of the normal intestinal flora, lactose is preferable to maltose.

Although maltase is formed before lactase, lactase is present at birth and becomes abundant as soon as milk is given and there is any need of it. The early appearance of maltase is, therefore, no argument in favor of the use of maltose instead of lactose. The presence of maltase in the blood is no argument in favor of maltose as a food. The maltase is in the blood to break down the maltose formed from glycogen, not to break down sugars in the intestine. It is impossible, moreover, for it to get into the intestine. The assimilation limit of lactose is, it is true, lower than that of maltose. This limit is, however, at least three times as large as would ever be given in a properly modified milk. The higher assimilation limit of maltose is therefore of no practical advantage. In spite of its higher assimilation limit, moreover, more maltose than lactose is excreted in the feces when equal amounts are given by mouth. The more rapid immediate gain in weight when maltose is added to a food poor in sugar than when lactose is added is of no importance, since the gain in both instances is almost entirely due to the retention of water. Even if it is true that the so-called "sugar fever" is really due to sugar, the fact that the rise of temperature occurs more often with lactose than with maltose does not count in favor of the use of maltose rather than lactose in the feeding of normal infants, because fever never occurs unless there is a diarrhea which shows some lesion of the intestine. Neither is the fact that large amounts of lactose cause diarrhea more easily than maltose and the dextrin-maltose preparations of much importance, because such large amounts of lactose should never be given. The less rapid breaking down and the consequently slower absorption of lactose than of maltose is of great importance in maintaining the normal fermentative flora throughout the intestinal tract. Few organisms other than those normal to the intestinal tract of infants can utilize lactose before it is broken down, many can utilize maltose. Lactose is especially suited to the growth of the *Bacillus bifidus,* the organism normally predominant in the

large intestine; maltose to the development of the *Bacillus acidophilus*, which, when in excess, may cause disturbance. It is not necessary, therefore, to bring forward the argument that lactose is the only sugar present in human milk and in the milk of other animals and that it must be therefore the natural sugar for an infant, because, in the light of the evidence just cited, there can be no doubt that lactose is preferable to maltose for the feeding of normal infants.

Finkelstein and Meyer believe that the diarrheal diseases of infancy originate in a functional weakness of the intestine, that this functional weakness is kept up and increased by fermentation, and that sugar is the special and primary cause of fermentation. Neither normal or abnormal acidification can take place without it. The fat is never involved primarily. It is injurious in that it causes an acid fermentation. The fermentation of the sugar is dependent on two main factors: The concentration of the whey, and the relative proportions of casein and sugar in the mixture. They conclude, therefore, that the principles on which the preparation of a food to combat intestinal fermentation depend are: A diminution in the quantity of milk sugar; a diminution of the salts through dilution of the whey; and an increase in the casein, with varying, and, under certain circumstances, not inconsiderable amounts of fat. They consequently developed a food to meet these indications, to which they gave the name "Eiweissmilch." This food is prepared with precipitated casein and buttermilk, after which it is boiled. Its composition is: Fat, 2.5 per cent.; lactose, 1.5 per cent.; proteid, 3 per cent.; salts, 0.5 per cent.

They claim that with this mixture the loose, green stools are quickly replaced by typical soap stools. One quart of this milk contains, however, only about 370 calories. Babies taking it suffer, therefore, from lack of nourishment. They advocate, therefore, the addition of malt sugar or the dextrin-maltose preparations to the mixture after the disappearance of the acute symptoms in order to avoid loss of weight and disturbance of nutrition. They claim that, on account of its more rapid absorbability, maltose does not cause a recurrence of the symptoms of fermentation.

Finkelstein and Meyer's arguments point strongly to sugar as the etiologic facor in intestinal fermentation. Their treatment of fermentative conditions with a food low in sugar and high in proteids is therefore a rational one. The substitution of dextrin-maltose mixtures for lactose also seems rational. It does not seem rational, however, to treat all cases in the same way or to give all babies the same food without regard to

their individual digestive capacities. The lactic acid in the buttermilk also seems irrational in that it is one of the products of the fermentation of lactose and, therefore, presumably one of the substances causing the disturbance in the intestine.

It seems wiser to take advantage of the main principles of this method of treatment of the intestinal fermentative conditions and avoid the disadvantages of a routine food and the unnecessary, even if not harmful, lactic acid. It is possible by using mixtures of precipitated casein, prepared according to Finkelstein and Meyer's method, water and cream to obtain any desired percentages of fat and casein with extremely low percentages of lactose and salts. Any of the dextrin-maltose preparations can then be added in any quantity desired. The use of this method of treatment in a considerable number of cases during the last year has convinced me that there is a variety of intestinal indigestion in infancy which is relieved by reducing the sugar and salts in the food to a minimum and giving large amounts of casein and that the dextrin-maltose preparations can be given to these patients sooner than lactose without causing a return of the symptoms. This type of intestinal indigestion may be either acute or chronic and is characterized by an increased number of stools of diminished consistency, green in color, often frothy, acid in reaction, and not infrequently containing mucus and fat curds. Unfortunately, however, precisely similar stools may be seen in other conditions in which the trouble is due primarily to bacteria and in which this method of treatment may do material harm. It is to be hoped that with increasing knowledge of the bacteriology of the intestinal tract in infancy some simple methods will be evolved which will make it possible to readily differentiate between the diarrheas due primarily to chemical changes in the intestinal contents and the disurbances of the digestive functions dependent on them and those due primarily to bacteria. At present it is extremely difficult to distinguish between them and correspondingly hard to know how to treat them.

There is a type of diarrhea in infancy, usually characterized by watery, green, foamy, irritating stools, but sometimes with discharges of mucus and blood, which is associated with the presence in the intestinal contents of large numbers of bacilli belonging in the group of which the *Bacillus perfringens* and the gas bacillus (Bacterium Welchii) are members. These organisms ferment the common disaccharids and liberate considerable amounts of butyric acid. Large amounts of sugar are, therefore, contra-indicated in this group of cases, maltose being more harmful

than lactose because it undergoes butyric acid fermentation more readily. This type of diarrhea yields most rapidly to buttermilk and mixtures containing living lactic acid bacteria with a small amount of lactose. The lactic acid forming organisms kill out the pathogenic organisms. Being themselves fermentative organisms, they cannot develop in a protein medium. A moderate amount of lactose must, therefore, be present in the food.

It has been shown by Theobald Smith, Kendall, and others, that when bacteria act upon carbohydrate and proteid substances they produce from the former fermentative products and from the latter putrefactive substances. The fermentative process takes precedence over the putrefactive if both carbohydrate and proteid are present together in the medium in which they are. The products of the fermentation of carbohydrates are practically harmless, while the products of the decomposition of proteids are actively toxic. In the diarrheal diseases due to organisms, such as the dysentery bacillus, which produce toxic substances from protein, it is therefore of great importance to have an excess of readily fermentable carbohydrate in the food to change the character of the bacterial activity from the proteolytic to the fermentative type. This is most easily accomplished by the feeding of the disaccharids which are preferable to the monosaccharids, because they are more readily procured and especially because they are less rapidly absorbed from the intestinal tract, and to the polysaccharid, starch, which, if given in sufficient amount to accomplish the desired result, is almost certain to disturb the digestion. Starch is broken down so slowly, moreover, that there is never a sufficiently great concentration of sugar at any time. Lactose is preferable to maltose for several reasons. It is, in the first place, more slowly broken down and absorbed and consequently exerts a more prolonged action. In the next place, few organisms, except those normal to the intestinal tract of infants, can utilize it before it is broken down by hydrolysis. There is also danger, as already pointed out, if maltose is given freely, of encouraging the overdevelopment of the *Bacillus acidophilus* and developing a suger intolerance.

CONCLUSIONS

Lactose is for many reasons preferable to maltose for the feeding of normal infants. There is a type of intestinal indigestion due to the fermentation of sugar in the treatment of the convalescent stage of which maltose is better borne than lactose. Maltose is contra-indicated in the

treatment of diarrheas due to the gas bacillus and similar organisms, and is less useful than lactose in the treatment of those caused by the dysentry bacillus.

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DISCUSSION

DR. HOWLAND said that it was apparent that more information was required as to the results of feeding dextrins. So far as he was aware there was very little experimental evidence from which conclusions could be drawn. In one German series in which pure dextrin had been used the results were so unsatisfactory that the subject had not been pursued further. With regard to the use of lactose in normal children, Dr. Howland did not believe that the attitude of those Germans who look on lactose as an improper addition to milk for artificial feeding was right, but he could not agree that the use of lactose in large quantities was a rational procedure in the treatment of infantile dysentery. Lactose in the quantities advised would be very likely to increase the diarrhea and this was a danger always to be kept in mind.

DR. ABT said that he had used the malt preparations for some time and the most striking thing was that normal children did very well so far as the gain in weight was concerned. He thought it was well known that practically all the preparations belonging to the malt-dextrin group would cause constipation, therefore, it was necessary to add some substance or substances to these preparations to overcome this tendency. When combined with lactose there was considerably less trouble from constipation. With regard to Dr. Morse's remarks about the bacteriology of the gastro-intestinal tract and sugar therapy and the results, it seemed to Dr. Abt that the whole subject of the bacteriology of the gastro-intestinal tract is still in an indefinite state, and he thought he voiced the sentiments of all in stating that little if any progress had been made in that respect. Men had without doubt done valuable work but they could not base any conclusions on it, nor could they classify intestinal disorders, much less prescribe sugars on the basis of the flora of the intestinal tract. Dr. Abt thought that too much importance had been given the sugars alone. It seemed to him that the ordinary normal child took equally well malt sugar, cane sugar and sugar of

milk; that was his experience. In both dispensary babies and those seen in private practice, changes from the preparations of malt to milk sugar and then to cane sugar did not influence their progress.

DR. FREEMAN said that he had been much instructed and pleased by the reading of the papers, and felt that anything that might limit the too general use of malt sugar was valuable. All babies should have a chance to thrive on normal feedings before being put on malt soup, and the tendency of some pediatricians is to put all babies on this latter food. The cases of scurvy we see now are largely in children who have been fed on these malt foods and the speaker thought that had the investigation of this Society on scurvy, which showed 60 per cent. of the babies to be fed on proprietary foods, separated those on malt foods, it would have found that most of this 60 per cent. had been fed on malt foods and a considerable proportion of the others on too little food. Maltose has its place in infant feeding but should only be used when good results cannot be obtained with lactose.

DR. HOLT spoke of the relation of maltose to the production of scurvy and said that it was incontestible that children fed on maltose for a long time did develop scurvy. He thought that for relieving constipation the liquid preparations of maltose were rather better than the dry preparations. Last year in studying the effects of different sugars he had thought that possibly the symptoms sometimes following the use of lactose might be due to bacterial contamination. Cultures made, however, showed that the hospital supply of lactose was practically sterile, as was also the cane sugar; but maltose preparations, both the dried and liquid, contained, on the other hand, large numbers of a Gram positive spore-bearing bacillus which also appeared in the stools of infants taking these preparations. Experiments on animals indicated that this was non-pathogenic. The organisms were killed only by quite a high temperature, boiling point for twenty minutes being required. That temperature would, of course, change the composition of the sugar. Much is yet to be learned about the variations in sugars and their use in cases of disordered digestion. He thought that the use of cane sugar in certain forms of diarrheal diseases was sometimes possible where both malt sugar and maltose were badly tolerated. This was the secret of success in the use of the canned condensed milk.

DR. LA FÉTRA said that pediatrists are very well agreed that milk sugar does harm in many cases of diarrhea. Among hospital patients especially, there is no doubt that most cases are improved when the milk sugar is discontinued and either cane sugar or one of the dextrin-malt preparations is substituted. During the last ten months he had been using not only cane sugar but the dextrin-malt preparations as well, and had obtained far better results in his diarrheal cases.

DR. COIT believed that there was a chemical difference, as well as a gross difference due to contamination, between the mother's sugar of milk and the commercial sugar of milk and, for that reason, he tried to get at the trusts who were marketing sugar of milk. Twenty-five years ago sugar of milk was made at one factory in Vermont by a man named Bennett. Later this factory was absorbed by the trusts. It was quite difficult to reach a hearing with the trusts: they did not want to talk or to correspond with Dr. Coit. Finally he was able to reach the ear of one of the officials of the trust and was treated with great courtesy. A chemist was sent for and came down and he had a three hours interview. They admitted the presence of bacterial toxins but they stated that their milk sugar answered the requirements of the pharmacopoeia. Dr. Coit said he

wanted evidence that the milk sugar contained no bacteria. Professor Leeds had carefully investigated the matter and he found that milk sugar was full of bacteria and also chemical impurities.

Never use more than 1 ounce; to increase its caloric value, add fat. Milk sugar was not trustable and, therefore, should be boiled. Better results were to be had when it was boiled than when it was not boiled.

The brand of milk sugar known as "XXX" was the finest and required the most delicate analytical work. It occurred in octahedral crystals and sold for 18 or 20 cents a pound. There were many grades of milk sugar. This "XXX" milk sugar was prepared by redissolving the ordinary grade, filtering through charcoal, and boiling down into these crystals.

DR. GRIFFITH remarked that he was one of the committee appointed by the American Pediatric Society to conduct the collective investigation on infantile scurvy in America, and that the report distinctly attributed many cases of scurvy to the administration of proprietary foods, a number of which were of the malt-sugar class.

DR. HAND said that he had never conducted a scientific investigation on the influence of sugar in infant feeding, but he always felt that the giving of lactose tended to produce diarrhea. These children, he thought, should be grouped according to the conditions presented. In private practice where milk sugar was used so much there was a tendency to produce constipation but this was on account of its diuretic effect. In private practice among children there was, as a rule, more trouble with constipation than there was among the babies in the hospital wards. Where a child was obstinately constipated the use of lactose or saccharose had a better tendency to regulate the bowels; they did not increase the tendency to diarrhea. It seemed to him that they should consider more the class of patients with especial regard to their general health.

DR. SOUTHWORTH said that Dr. Morse had spoken of the disadvantages of the use of starch. Dr. Southworth had also long maintained that starch could be abused in feeding infants. Nevertheless barley water and other cereal diluents had been employed largely during the last decade for infants who were not doing particularly well with plain water as the diluent of the milk.

Dr. Howland had stated that a group of children fed with dextrin had all died. This did not mean by any means that they were injured by the dextrin, for one of the well known malt sugar preparations contained 60 per cent. dextrin and could not have been widely used if it was in any way injurious. Very little attention had been paid until recently to the presence of dextrin in the maltose-dextrin preparations. Dr. Southworth said he was very much interested in hearing what Dr. Abt had to say regarding the use of the dry malt-dextrin mixtures and the statement that they were constipating rather than laxative in their effect, for that had been his own experience. The semi-fluid preparations on the contrary are laxative.

DR. MORSE said that his object in looking into the question of maltose in infant feeding was to find out what basis there was primarily for the wave of this feeding which had gone over foreign countries, then started in the middle west of the United States and which had finally begun to work its way east. The statement is often made that the milk sugar of cows' milk is not the same chemically as the milk sugar of mother's milk. For such a statement he could find no chemical basis; chemically they were the same. With regard to the statement made by Dr. Coit regarding the toxic bacterial products of milk sugar and the advantages of boiling, it was Dr. Morse's idea that boiling did not destroy the toxic

products although boiling might destroy, and probably did destroy, the bacteria. In Boston during the past two years Dr. Kendall had been working on The Floating Hospital on the bacteriology of the acute diarrheal diseases of babies during the summer months, and on his findings had made certain suggestions regarding the treatment of these cases, one of them being the immediate use of lactose by the mouth in the cases due to the dysentery bacilli. The staff of the Floating Hospital felt that their results were better in this way than they had been in the past. Dr. Morse had used this same line of treatment at the Children's Hospital and had felt not only that it did no harm but that it apparently did good. It must be remembered in this connection that other organisms than the dysentery bacilli can cause diarrheas in which the stools consist of mucus and blood. This was the case last summer in Boston when the prevailing organism was the streptococcus. In other instances the causative organism may be the gas bacillus. In this case lactose would presumably do harm. It is very difficult, therefore, to draw conclusions as to the effect of treatment in the diarrheal diseases in infancy unless the causative organism is known.

THE EFFECTS OF HEATED AND SUPERHEATED MILK ON THE INFANT'S NUTRITION (RECENT INVESTIGATIONS)

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The physician will always be influenced in his teaching and practice by the results of his clinical experience, and while his teaching and practice should be justified by laboratory investgation and the results of research, his final judgments should also be influenced by clinical experience, always recognizing the difference between the ideal and the practical.

It seems somewhat paradoxical that I should array myself with those who endorse the heating or superheating of milk for infant feeding. I must state that no one could be a stronger advocate of raw milk, when it is ideally clean and safe, in the feeding of normal children. However, I have frequently been driven to the expedient of refining milk at efficient low temperatures and at high temperatures in treating sick infants and sometimes boiling it for several minutes, and I have been compelled to conclude that the heating of milk is not the menace to its nutritive values that champions of raw milk would have us believe.

My own experience covers a period of twenty-five years and my records include about six thousand feeding cases which, from the standpoint of heated milk and clean raw milk, I shall hope to study and report upon in the near future.

I shall not now offer any of my own conclusions, but refer to an English investigator, Dr. J. E. Lane-Claypon, authorized by and working under the direction of the British Local Government Board. The report has just been published (February 24, 1912) by Dr. Arthur Newsholme, Chief Medical Officer of Great Britain, and embodies the results of an inquiry undertaken in connection with the parliamentary grant for scientific investigations. The report is upon the available data in regard to the value of boiled milk as a food for infants and young animals and is presented in five parts.

Part I is an introduction in which the investigation is justified upon the intimate connection between the artificial feeding and excessive mortality among infants. The great superiority of breast milk or of milk of

the same species, over milk obtained from any other source, as a food for infants and young animals is established by experimental evidence and clinical experience and emphasizes the opinion that infants should be fed at the breast unless there is an urgent reason to the contrary.

The introduction includes the author's plan for the investigation of the problem, which is dealt with under two main divisions:

1. The comparative nutrition value of raw and boiled milk of the same species.

2. The comparative nutritive value of raw and boiled milk of a foreign species.

Both divisions are influenced by the factors of *age of the young animal or child, the quantity and quality of the milk given and the environment or social condition.* The most important aspect of division two concerns the artificial feeding of infants with raw or boiled cows' milk.

The clinical requirements for the elucidation of the problem are a large number of healthy babies, under medical supervision, and the known social environment, who were fed for prolonged periods upon raw or boiled cows' milk.

Infant consultations provide the material of this type, from which sick babies were excluded, being referred to a hospital. The material used was under medical supervision, accurate records kept, the infants' food regulated and nutritive conditions noted. Further, the babies were visited in their own homes periodically, so that the social environment was known.

Among the material investigated, the most important was that courteously placed at the disposal of the author by Professor Finkelstein and Dr. Ballin, the Director of the Municipal Infant Consultation in Berlin.

Part II deals with experimental evidence gathered from the work of various investigators on the relative value of raw and boiled milk of the same species as obtained from experiments upon lower animals. This includes the work of Gerlach, who, after failure with boiled milk, was successful after the addition of mineral salts to the boiled milk. It includes the work of Hittcher along the same line, in which he restored to boiled milk the quality of clotting with rennet by the addition of certain salts.

Reference is made to the work of Bang in Denmark, who has studied hundreds of cases, and has found the feeding of boiled milk entirely satisfactory. The experiments of Price and Doane in this country, are

also estimated in the author's conclusions. The work of Bang and Hittcher give strong evidence that no serious loss of nutritive value is produced by boiling the milk of the same species.

The experimental evidence on the nutritive value of raw and boiled milk of a foreign species as applied to the lower animals includes the work of Bolle, Bartenstein, Bruning and Moro upon guinea-pigs and concludes that these animals are not suitable ones upon which to carry out feeding experiments.

The work of Keller on mice is referred to, and the author's own work on rats at the Lister Institute for Medical Research, the work of Bruning and Moro on rabbits, and the work of Rodet, Keller, Bruning and Moro on dogs, Moro showing that dogs fed on human milk remained alive, but were in a very miserable condition, whereas dogs fed on cows' milk did extremely well. These results by the same observer on rabbits show that it is very important to use the species of animals whose milk is suitable for the species whose growth is being investigated.

Reference is made to the work by Chamouin, Grunbaun and Vincent on kittens, and the work of Bruning and Bamberg on pigs. Reference is also made to the work on identical lines with goats by Bruning and Bruckler, in which it was found that goats did fairly well on cows' milk, but results are very inferior to those obtained with mothers' milk, and that there was a distinct advantage in giving it boiled.

Summarizing the results of experiment on lower animals, the author states:

1. That there is no evidence to show that boiled cows' milk is markedly inferior to raw cows' milk, as a food for young calves, at any rate after the first two days of life (cp. Bang).

2. That the salt content is of great importance (cp. Hittcher and Gerlach).

3. That, if young animals are few on the milk of a suitable foreign species, they appear to thrive somewhat better if the milk is given boiled, than if given raw, the only exception being in the case of germ-free milk (cp. Bamberg).

4. That in those cases where the health of the animals was inquired into, after the cessation of the experiment, no difference could be detected in the animals fed by different methods of artificial feeding.

5. All the animals fed by different methods of artificial feeding were inferior to the breast-fed animals, both at the time of the experiment and afterwards.

Part III includes clinical evidence as adduced by many authors who have worked with scanty material in institutions and hospitals. The author regards most of this evidence as of doubtful value since most of these children show definite wasting; some of them had reached the later stages of atrophy, and believes that its importance is to show how far the metabolism of such children is directly comparable with that of healthy children, but as to the relative adjustability and nutritive value of the food given, it would be more likely to be more pronounced in the case of a sick than of a healthy child.

These conclusions are emphasized by the facts:

1. That different observers are not agreed upon the relative value of raw and boiled milk in the treatment of atrophic children.

2. It is usually difficult in hospital practice to keep the children under observation for a sufficiently long period to study to the full the effects of the observations made in the hospital.

3. The variation in the details in the source and preparation of the milk given, and as to the understanding of what sterilized milk really is.

4. The variations under different observers upon different classes of babies in the quality of the milk use. It is only by feeding babies on raw and boiled milk of the same quality that any reliable evidence can be obtained.

The authors referred to who, in institutions, fed infants on boiled milk of the same species were Moro, L. F. Meyer, Potpeschnig, Bering, Müller, Finkelstein and Professor Thiemich, of Magdeburg. The work of the latter, although yet unpublished, was available to the author. He states that: "In my wards the milk of all the new wet-nurses is given boiled only until Wassermann's and Stern's reactions have been carried out."

On this system he has tabulated a great number of children who have improved as advantageously on boiled human milk as happens with raw human milk. In a number of cases raw and boiled human milk have been given alternately and systematically for various periods with the same results.

The report deals also with the clinical evidence in regard to infants fed on raw and boiled milk of a foreign species, and the following authors are quoted: Ulig, Leeds and Davis, Monrad, Variot, Czerny, Halipre, Hahlfield, Vincent and Finkelstein. The latter investigator carried on his work over prolonged periods, on both healthy and atrophic children, as well as on those suffering from acute disturbances. Finkelstein con-

cludes that "no definite distinction between the results obtained by feeding on raw and boiled milk respectively could be detected." If Finkelstein's figures as seen in Group I (a) are examined carefully, it will be seen that there is a balance in favor of boiled milk.

Metabolism experiments of Bendix, Lange and Koplik are given. Reference is made to the alleged production of rickets and infantile scurvy by boiled milk.

In the summary of the experimental clinical evidence which was obtained from institutions and hospitals, the author concludes that the balance of evidence may be said not to show any decided superiority on the side of either raw or boiled cows' milk as a food for infants.

Part IV deals with the method and results of working up the Berlin material and is treated under the heads of

The Source of Material.
The Milk Supply for the Consultations.
The Notes taken at the Consultations.
The Selection of Material.

Under this last head, it was found necessary to deal with two main series of infants:

1. Healthy babies of the average artisan class fed on milk in various forms in order to have a control consisting of the average baby.

2. Healthy babies of the same class but fed only on boiled cows' milk in order to study the difference, if any, produced on the average baby of the class by feeding it exclusively on boiled milk, as compared with the infants of class 1.

In considering the babies of this first class, it appeared that far the larger portion were fed on the breast, and that all the others were fed on boiled cows' milk. There were a very few cases of mixed feeding on the breast and on boiled milk, lasting over a few weeks.

This was of course foreseen, since the material which was to be used was that of an infant consultation where the babies were, if possible, fed on the breast and failing that, on boiled milk.

Hence, if the babies attending the consultation had been taken seriatim, regardless of the variety of feeding they were receiving, and had been utilized for preparing control statistics under the first head given above, the results would have been complicated by the presence of a considerable number of babies of the second class which was required to be a class by itself. It was decided to exclude from the control series all babies who had received less than four months breast feeding.

The author then makes an analysis of the material used, and presents very complete results in tabular form, followed by a critical review of the statistical methods employed.

Table I shows the age of first attendance and of leaving the consultation of the babies of the control or breast-fed series.

Table II shows the age of first attendance and on leaving the consultation of the babies of the boiled cows' milk series.

Table III shows the average weights of the babies of the control or breast-fed series, grouped in periods of eight days and the number of observations made.

Table IV shows the average weights of the babies of the boiled cows' milk series, grouped in periods of eight days, and the number of observations made.

The average weights found and shown in Tables III and IV are plotted on Diagram I.

About 12,000 observations were made.

Analysis of Diagram 1: Diagram I shows that a considerable divergence between the two curves starts in the early days of life and continues well marked up to about the 208th day, after which it disappears fairly rapidly. The possible difference between the average weight of breast-fed and boiled cows' milk fed babies of the same age being due to error of sampling, was carefully examined and deduction drawn.

Table V shows distribution of 345 observations on the weight of 504 infants in relation to the food between the 137th and 144th day of life, which is used to check up possible error in conclusions.

Table VI shows the distribution of the observations of the feeding of infants in relation to the wages.

Table VII shows the percentage of the rate of increase for each period of eight days of the babies of both series up to the age of eight months. The results given in Table VII are plotted on Diagram II. Both series show an extreme irregularity in the rate at which the weight increases, and after the first two estimations, it would be difficult to point out any marked difference between the values of the two series.

Table VIII shows the percentage of the rate of growth of the babies of both series, starting from the second eight-day period of life, the control series being the breast fed babies, and the other series being babies which were fed on boiled cows' milk. The results shown in Table VIII are plotted in Diagram III, which shows that as regards the rate of growth, there is little to choose between the two series. The babies fed

on boiled cows' milk doubled their weight at the 185th-192d day, or a fortnight earlier than the breast-fed babies, but they started with usually a lower weight.

Table IX shows the percentage of the relationships between the average weights of the babies of the two series: Series I consisting of the breast-fed babies, and Series 2 consisting of babies fed on boiled cows' milk. This shows a more favorable result than those obtained in the feeding experiment on animals which received the milk of a foreign species, which renders it doubtful whether the result could be surpassed by feeding babies on raw cows' milk.

Table X shows the average weights and the number of estimations of 78 babies who were never breast-fed, and of 41 babies who were breast-fed for eight days or less.

Table XI shows the average weight of 130 babies, exclusively breast-fed up to 200 days of age, and of 119 babies of whom 78 had never been breast-fed and of 41 who were breast-fed for less than eight days.

The figures obtained by estimating the weights of the 130 breast-fed and the babies fed exclusively on boiled cows' milk show the main characteristics as the curves of the original series of babies as plotted in Diagram I. The divergence is more accentuated, but the tendency of the two curves to approach one another at about the 200th day begins to appear after the 160th day. The average weights and the results are plotted on Diagram IV.

Table XII shows the percentage of growth of 119 babies who had never been breast-fed, and of 130 babies who were exclusively breast-fed, starting from the average weight at the end of the 16th day of age, and continuing up to the time at which they doubled their weights. Both breast-fed babies and those fed on boiled cows' milk doubled their weights at the 193d-200th day of life. This is plotted on Diagram V.

SUMMARY OF RESULTS OBTAINED IN PART IV

The Berlin figures dealt with in this part of the report show that given circumstances similar to those of the consultation from whence the figures are taken:

1. Infants fed on the breast show a higher average weight than infants fed on boiled cows' milk up to about the 180th-220 day of life. After this age the difference in average weight disappears.

2. This difference must be attributed to the method of feeding, and not to differences in the social condition of the infants.

3. The difference in average weight is most marked in the first 16 days of life. This difference must be attributed to the different method of feeding, and not to any possible "error of sampling."

4. After the first sixteen days the average increase in body-weight is almost identical in both series of babies.

5. The deficit of average weight of the babies fed on boiled cows' milk below those fed on the breast does not reach 10 per cent. at any period.

PART V. SUMMARY AND CONCLUSIONS

The balance of evidence both experimental and clinical points in the main to the same conclusions. Both lines of research show:

1. That there is apparently no serious loss of nutritive value produced by feeding an animal on boiled milk derived from an animal of the same species. At the same time it must be pointed out that the published evidence on this point is scanty.

2. That, when an animal is fed on the milk of another species, the milk from which has been found to be suitable for this purpose, such small differences as have been found in the nutritive values of raw and boiled milk have been in favor of boiled milk.

3. That the milk of the same species has a considerably higher nutritive value for that species than the milk of any other species so far investigated.

The evidence dealth with throughout this report emphasizes very forcibly the importance of breast-feeding for the young of all species, and shows the special importance of breast-feeding during the early weeks of life.

Where artificial feeding has been employed in animal experiments, boiled milk of a foreign species has given more satisfactory results than similar milk raw. The Berlin figures dealing with infants fed on boiled cows' milk, give extremely favorable results, and in view of the evidence collected in this report could scarcely be expected to be surpassed had raw cows' milk been used.

It may be again pointed out that the Berlin babies who are artificially fed in connection with the consultation receive milk of a known excellent quality. The excellence of the results obtained in Berlin are almost certainly largely due to the care and supervision exercised at and through the consultation.

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DISCUSSION

DR. HAMILL said that he wished to ask a question which he thought important, namely, whether the determination of the satisfactory results was based solely on a gain in weight. As far as he heard the report, no other criteria were offered. He thought it very unfortunate that the success of infant feeding should be based solely on a gain in weight, since there are so many other factors which must be taken into consideration in determining the condition of nutrition of the child. Condensed milk and other proprietary foods, which are absolutely inadequate as foods, will frequently produce striking increases in weight; and Dr. Hamill, therefore, felt that it was imprudent for this Society to permit the impression to go abroad that it approves this very common but unsatisfactory method of determining the satisfactory nutrition of the child.

DR. ABT said that the profession within recent years was coming to a point where they believed in having the milk to be fed infants boiled; little babies would digest the milk more readily and thrive better, with less danger of rickets or scurvy, if the milk was boiled. They seemed to be even more fortified against scurvy when the milk was boiled than when given orange juice. It seemed to him that the effect of boiling milk was practically the same as the boiling of other raw foods; it made it more digestible, the same as cooking meats. There was no doubt in his mind that the boiling of milk made it more digestible.

DR. NICOLL, in speaking about the toxins found in sugar of milk, did not believe that what Dr. Coit had stated should be allowed to go out as an expression of the sentiments of the American Pediatric Society, unless Dr. Coit had a definite reason for his statement.

DR. EATON called attention to one point that had not been brought out clearly —the physiological and chemical condition of the milk; milk might be or might not be boiled, but whatever was done with it, it should be brought up to a certain standard.

DR. TALBOT believed that if more attention was given to obtaining clean milk there would be less need of boiling it.

DR. SOUTHWORTH said that one or two years ago Vincent of England published a brochure on the feeding of infants with unsterilized and sterilized milks, claiming that if they were fed on sterilized milk in hot weather they would be in a worse condition at the end of twenty-four hours owing to the growth of putrefactive bacteria in such milk. The crux of the matter was that in England the poor had no ice; therefore sterilized milk was worse than the ordinary unboiled milk which soured but had in it the protective lactic acid bacilli. There was a reason for bringing out such a report in England which did not apply in this country where we had an abundance of ice. Similarly the investigations reported by Dr. Coit were doubtless prompted by conditions in England.

DR. FREEMAN replied to Dr. Talbot's remark, and asserted that no raw milk produced carried any absolute safety. That such safety could only be obtained by pasteurizing or sterilizing the milk in nursing bottles at the home. No dairy methods at present in use, although they reduce the danger, can eliminate the danger from disease carrying germs.

DR. CHURCHILL thought that it was possible to obtain clean enough milk, milk with low bacterial count, for infant feeding, milk that was not necessary to pasteurize or to boil. Last summer in Chicago they had a very low mortality rate and this resulted simply from feeding babies on clean milk and many of these

babies lived in the slums. This was due to the fact that the babies were furnished with a known clean milk and, after the giving of this clean milk, there came the follow-up nurse. It came down practically to the education of the people, teaching them how to modify the milk and how to keep the milk clean. Dr. Churchill thought that it was perfectly safe to give these babies milk that was not pasteurized or boiled, if it was clean and properly cared for after delivery.

Dr. Kerley said that the discussion reminded him of ten or twelve years ago, because it was just directly opposite to the remarks made at that time. It was then claimed that raw milk was the only suitable food for a child. To this practically all agreed except Dr. Freeman, who adhered to the necessity of pasteurization of milk for infant feeding. Regarding the heating of milk, the important point was not that it was boiled but what was cooked with it. There is no question but that the cooking of milk with certain other substances, such as starch and the alkalies, makes it much easier of assimilation. This he had demonstrated in hundreds of instances in the use of malt soup mixtures; also after cooking, barley, milk sugar and milk make a successfud diet for those who can not take milk in its raw state.

Dr. Griffith called attention to the fact that the conclusions which might be drawn from the charts exhibited were of a distinctly harmful nature. They might be construed to indicate that children thus artificially fed thrived better than those on human milk. None of us believe that this represents the true state of the case, and all of us desire to do all in our power to advance the growing sentiment in favor of breast feeding. He realized that Dr. Coit certainly shared this sentiment, and he thought that the apparent teaching of the article reviewed should not pass without criticism.

Dr. Knox said that the question of boiling milk for infant feeding was a most important one. Boiled milk should not be used after a certain time, as the boiling destroyed the natural curding of sour milk, and so in a way produced a dangerously masked product, as it might contain a large number of poisonous bacteria without changing the physical character or appearance of the milk. Heating milk, however, was the greatest help in destroying the possibility of conveying infectious diseases such as typhoid fever, tuberculosis, scarlet fever, etc. A number of epidemics of these diseases have been traced to excellent dairy farms. At present the only method of surely eliminating danger from these sources seems to be to heat the milk.

Dr. Heiman believed that there must be a good reason for such diversity of opinions such as had been shown in the discussion and that time alone would solve the problem confronting them. They were all advocates of percentage feeding for a time, and then they tried to get away from it for certain reasons, because they found, in their clinical experience, that occasionally rickets followed the use of raw milk as quickly as the use of milk that had been boiled. This was undoubtedly due to cow's milk itself and not to the boiling. There seemed to be some faulty metabolism. If this was a fact it seemed to him that it would be much safer to boil all the milk intended for infant feeding.

Dr. Adams asked to be allowed to say a word in endorsement of what had already been said. There was a tendency among women, particularly among the better class of people, not to nurse their babies and if there should go out from the American Pediatric Society a dictum that it is safe to feed babies on boiled cow's milk, this would be a retrograde step, and should not be countenanced. When he began the practice of medicine boiled milk was generally used for babies and

especially among the working classes. They would go back to it if the statement was made that by boiling milk there were certain advantages over the breast-feeding. If such a statement were sent out as authoritative from the American Pediatric Society, it would also have a bad influence on the general profession. He said that they should be very careful what they endorsed. Great efforts were now being made to induce mothers to nurse their offspring. Before the child was born the expectant mother would say that she did not wish to nurse her baby. In England they did things that could not be done in this country. Certain articles of diet for adults were given to children there which would be dangerous to give here, such as cabbage to infants two years of age or under. Dr. Coit should not have so much confidence in the results he had obtained from other observers. It was like Dr. Wright's opsonic index; by its use everybody was to be cured. It was suggested that he give up the practice of medicine and crack stones on the railroad in order to make a living, as only a limited number could become proficient in such blood-work. One should be very careful about being too enthusiastic in accepting these reports unless he had sufficient data at hand. We all remember how quickly the opsonic bubble burst.

SERUM TREATMENT OF PNEUMONIA

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During the past few years many new methods for the treatment of that very fatal disease of infancy, pneumonia, have been instituted, but few of these have been markedly successful. Many of us believe that the use of out-of-door air has done more to limit the mortality of pneumonia than has been demonstrated for any of the treatments based on laboratory investigation.

Of the three treatments that come under this class one may mention the use of leukocyte extracts advocated by Dr. Hiss; the use of vaccines either commercial or autogenous, and, finally, the use of the serum.

The leukocyte extract of Hiss has produced some striking results, but has not as yet had sufficient use, I believe, to determine accurately its value. But in a report issued by Hiss and Zinsser[1] in 1908, they describe eight cases with recovery and with a reduction of temperature usually within two to four days after the injections were begun. These injections were repeated daily.

Vaccines, particularly autogenous vaccines, have been considerably used and some of the reports are quite favorable, but Stoner,[2] who has collected 155 cases of pneumonia, in which the patients were treated with vaccines, reports a mortality of 12.9 per cent. Howland and Hoobler report fifty cases, mostly in young children with bronchopneumonia, and some older ones with lobar pneumonia, treated with stock vaccines, but with no favorable results. A few cases also were treated with autogenous vaccines with similar results.

In going over the literature it has seemed to me that the results obtained from the so-called Romers' serum, a pneumococcus serum, have been in general very favorable. Thus Kriske[3] reports ten cases in children from 9 months to 10 years of age in which he noted a distinct improvement after the administration of the serum and all the children recovered.

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1. Hiss and Zinsser: Jour. Med. Research, 1908, xix, No. 3, p. 321.
2. Stoner: A Résumé of Vaccine Therapy. Am. Jour. Med. Sc., 1911, cxli, 186.
3. Kriske: Zur Serumtherapie de kruposen Pneumonie. Med. Klin., 1908, iv 1881.

May[4] reports good results in twenty cases with increased leukocytosis. Monti[5] used it in twelve cases with decided benefit, while Knauth,[6] Linderstern,[7] Tunher[8] and Crux[9] used it with favorable results. Brunning[10] treated six patients with falling temperature, slowing of the pulse and general improvement after the administration of the serum. All these observers used a dosage of about 10 c.c. for children and 20 c.c. for adults.

Morse, in 1903, reported to this society eight cases in which the patients were treated with 5 c.c. of pneumococcus serum every four hours, or about 30 c.c. daily, and concluded that the treatment "had no effect on the duration of the disease, the course of the temperature, the rate of the pulse and respiration or the progress of the local condition. Complications occurred at least as frequently as is usual. Death occurred in an unusually large percentage. The serum, while it apparently did no good, certainly did no harm."

On account of the usually favorable results of treatment with antipneumococcus serum it seemed worth while to try it in a series of cases, using alternate cases as controls. This work was undertaken at an institution where the children have poorer reaction to disease than is usual in private practice, and where under any form of treatment many children go on after pneumonia with a condition of unresolved pneumonia which persists for week or months.

The cases admitted to this series were in patients showing a fairly high temperature with good signs in the chest. One of the injected patients had a severe pneumonia complicating measles, another measles-pneumonia being used as a control. This patient showed no good effects from the serum and finally died of general septic conditions and endocarditis. Three patients injected are not included in this paper; two that were moribund when injected and were injected simply to see whether the serum might help them. One of these was rigid and comatose and made no cry when the large needle was thrust into the abdominal wall and

4. May: Ueber die Wirkung des Romerschen Pneumokokken-serums bei der kruposen Pneumonia mit besonderer Berücksichtigung der Leukocyten. München. med. Wchnschr., 1908, lv, 2140.

5. Monti: Arch. f. Kinderh., 1908, xl, 45.

6. Knauth: Deutsch. med. Wchnschr., 1905, No. 12.

7. Linderstern: München. med. Wchnschr., 1905, No. 39.

8. Tunher: Wein. med. Wchnschr., 1906, No. 11.

9. Crux: Zwolf Falle von Lungenentzundung im Kindesalter mit Romer's Pneumokokkenserum behandelt. Deutsch. med. Wchnschr., 1908, xxxiv, 16.

10. Brunning: Kinderpneumonie und Pneumokokkenheil-serum. Deutsch. med. Wchnschr., 1911, xxxv, 42.

died within four hours after the injection. In the other similarly hopeless case the patient died within twenty-four hours after injection. I also injected an adult who recovered.

The first seven of the patients were injected with a simple pneumococcus serum, a large dose, 100 c.c., being injected and in some cases repeated. The injection was done by means of a buret (Fig. 1) made for salvarsan injection and a rubber tube with a glass section near the needle and a very large needle, this being necessary as the blood serum will not flow freely through a small needle. The injections were all made into the

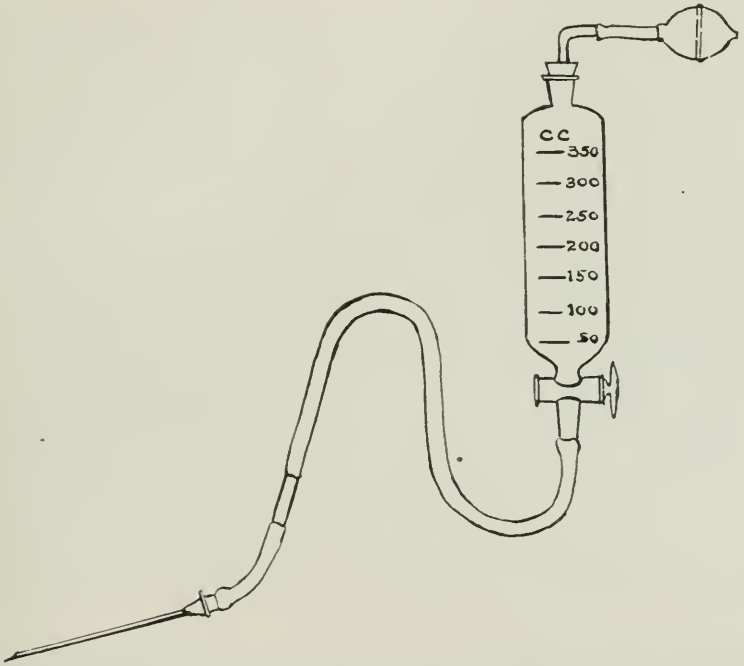

Fig. 1.—Showing apparatus used for injecting antipneumococcus serum.

anterior abdominal wall and it was found that by keeping the end of the needle in the fascia below the skin and gradually advancing this rather long needle 100 c.c. could be readily delivered with one penetration of the skin. Pressure was made in addition to that of gravity by the use of a rubber bulb attached to the buret.

The first seven patients received 100 c.c. of pneumococcus serum, while the last eight cases received 50 c.c. each of pneumococcus and

streptococcus serum. This serum was that of the New York Board of Health and I am indebted to Drs. Park and Nicoll of this department not only for the serum, but also for advice as to its use.

In none of the cases was there any evidence of irritation at the point of injection. The serum was rapidly absorbed and there was no inflammatory disturbance. In all of the cases, on the other hand, the injections were followed by urticaria, sometimes appearing on the following day, often ten days later, but without fever or general disturbance. In one case in addition to the urticaria an ankle joint was swollen, hot and

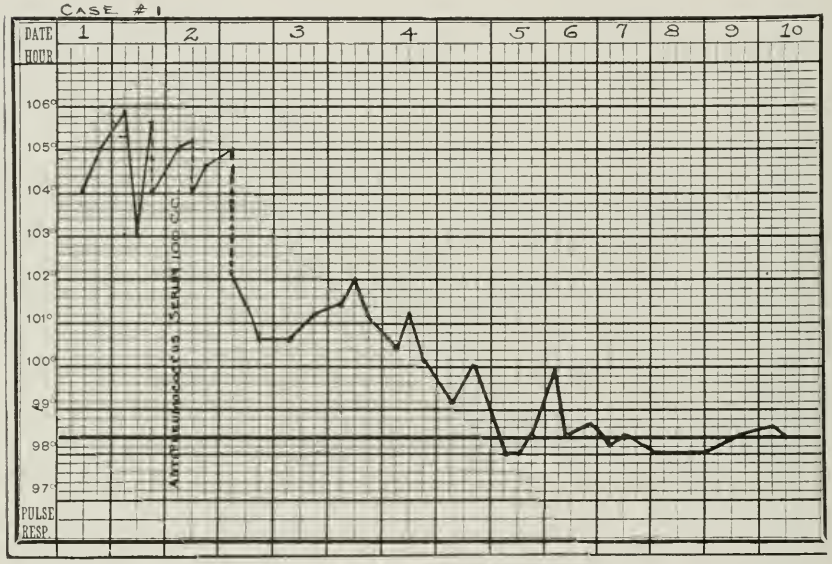

Fig. 2.—Temperature curve in Case 1, showing effect of injection of antipneumococcus serum on second day.

painful, but this subsided in twenty-four hours and was accompanied by little rise in temperature.

The children injected varied in age from 2 months to 3¼ years, the average age being 20 months, while the controls ranged in age from 3½ months to 3½ years, with an average age of 11 months.

As to the effect of the serum, there was in many cases an immediate change in the appearance of the child. Children that looked septic, were apathetic, with anorexia and a pale blotchy complexion, in several cases after the injection, had a good color, were brighter, took the feedings

better and seemed much improved, although the condition in the lung was usually unchanged or perhaps spreading.

Before going into the general effect of this treatment I would like to call attention to charts of several cases with marked results, to indicate that in some cases the serum seemed to be of real benefit.

Case 1 was a child that had appeared very sick, the temperature ranging from 103 to 105.8 F., and being 105.2 F. at the time of the injection (Fig. 2). The physical examination showed crepitant râles, increased voice and high-pitched breathing over the upper part of the

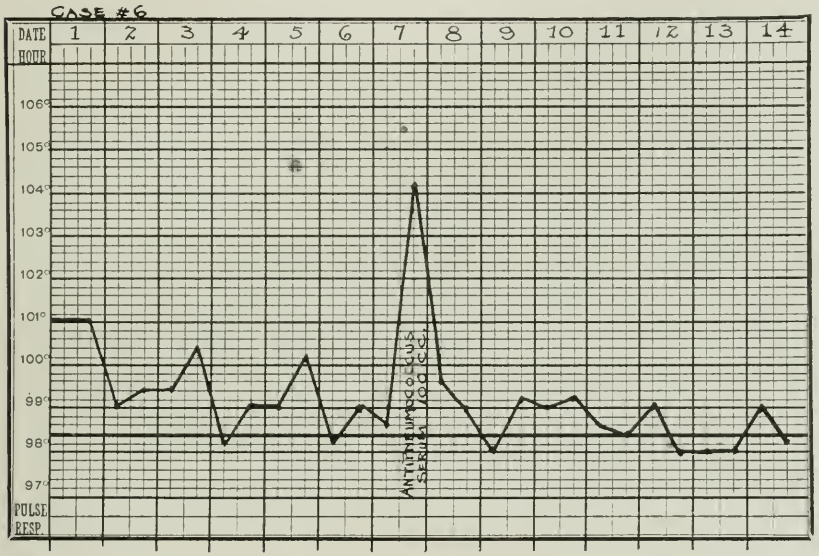

Fig. 3.—Temperature curve in Case 6. Injection of antipneumococcus serum on seventh day.

right lower lobe and over the right middle and upper lobes. After the injection the temperature immediately dropped to 102 F. and then gradually to normal, reaching that point three days after the injection and remaining normal after the fourth day. This injection was made on the second day of the disease and on the following day the signs showed an involvement of the posterior portion of the right lung, while on the third day after the injection and the fourth day of the disease the signs in the chest cleared up. This was fortunately the first injection case and made a very favorable impression on the people at the institution.

Another striking case was Case 6, in which the patient suddenly had a temperature of 104.1 F., with cough and cyanosis. On examination of the chest in the left subscapular region there was dulness, bronchial breathing, sharp subcrepitant râles, with harsh breathing and crepitant râles lower down, while on the right side there were sibilant râles. After injection the temperature dropped immediately to 99.6 F. (Fig. 3) and never rose, and the signs in the chest gradually cleared up. This seemed like a very wonderful result, but our control patient with no serum did exactly the same thing.

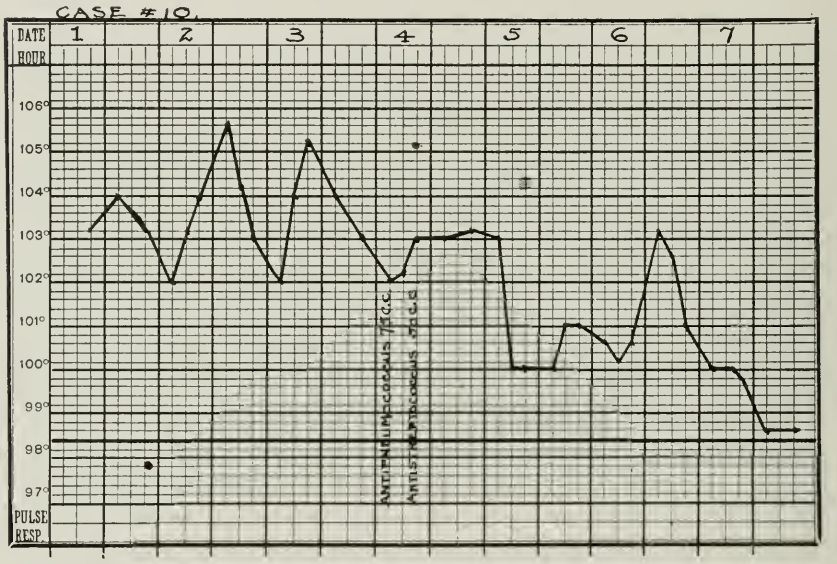

Fig. 4.—Temperature curve in Case 10. Antipneumococcus and antistreptococcus serum on the fourth day.

In Case 10 the child was injected on the fourth day after admission to the hospital, where it was brought on account of convulsions. At the time of injection it had bronchial breathing and crepitant râles over the right upper lobe and the temperature was 102.2 F. (Fig. 4). The temperature reached normal three days after injection. Some signs, however, persisted, but four days after the injection the chest showed only slight dulness at the right apex posteriorly and ten days later when the child was sent out of the hospital the chest was clear.

A very striking case was Case 11, in which the patient had run a steady temperature from 103 to 105 F. (Fig. 5) for four days before

injection. At that time the temperature was 104 F., and over the right lower lobe there was high-pitch respiration and fine râles, and pneumococci were obtained from a throat swab. After injection the temperature rapidly declined and reached normal in three days. In this case the leukocytosis, which was 15,000 at the time of injection, was the same on the following day, but on the second day was reduced to 8,800, while the polynuclear leukocytes changed from 41 per cent. at the time of the injection to 47 per cent.

These cases I have given simply to show that in some cases there was apparently a good reaction from the serum.

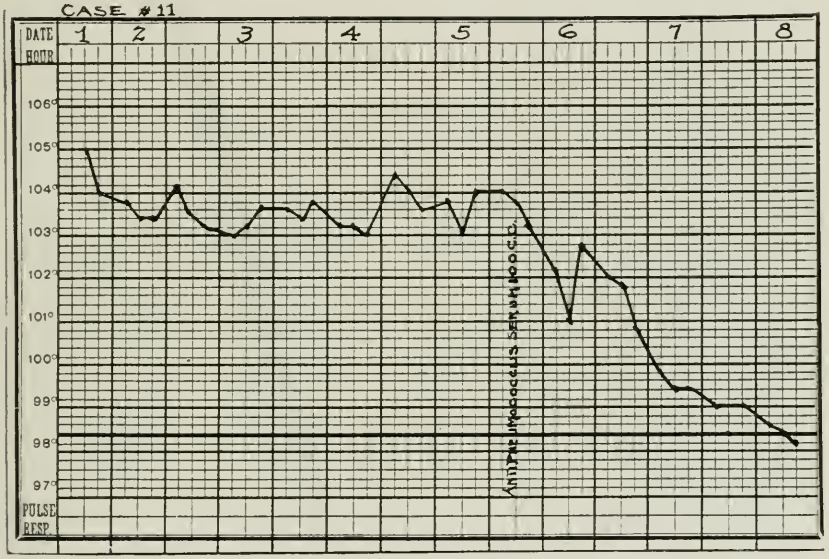

Fig. 5.—Temperature curve in Case 11. Antipneumococcus serum on the fifth day.

The improvement in the well-being of the children has been commented on by other observers and is not always followed by recovery.

The effect on the temperature in some cases was marked. In seven cases there was a reduction in temperature after injection, while in eight cases there was no evident effect.

The effect on the process in the lungs was interesting for, as I have said, in some cases in which there seemed to be an improvement in the general condition of the child, the lung condition either showed no improvement or spread. Where there was a marked reduction in tem-

perature from the injection the lung signs did not spread materially and often cleared up quickly.

The effect on the leukocytosis was studied in eleven cases (see table), most of which were injections of combined pneumococcus and streptococcus serum. These showed usually a reduction in the leukocytosis, although in one case the leukocytes increased from 10,000 to 18,000 with a reduction in the polynuclear leukocytes from 70 to 44 per cent. The average of the eleven cases was a reduction in leukocytes from 25,790 to 19,333, and a reduction of polynuclear leukocytes from 67 to 63 per cent.

RESULT OF BLOOD EXAMINATION AT TIME OF INJECTION AND TWENTY-FOUR HOURS LATER IN ELEVEN CASES

At Time of Injection		One Day Later	
Leukocytes	Percentage of Polynuclear Leukocytes	Leukocytes	Percentage of Polynuclear Leukocytes
58,000	84	18,400	64
17,800	75	11,000	69
24,400	42	21,760	79
14,000	75	14,000	74
15,000	41	15,500	47
26,000	86	17,400	48
34,000	85	36,000	95
10,500	70	18,000	44
16,000	27	12,000	40
40,000	73	21,000	70
28,000	76	27,600	71
283,700	734	212,660	701
*25,790	67	*19,333	63

*Average of the eleven cases.

so that the average result is not very striking. A more striking result, but on too few cases to draw any conclusions, is found by examining the three cases in which the counts were made on the third day. These show an average reduction from 29,667 on the first day to 15,300 on the second day, and of 11,933 on the third day, while the polynuclear leukocytes averaged 51 per cent. on each of these days.

The effect of the injections on the duration of the disease may be studied in those patients who recovered. In these it is found that the duration after injection, as shown by fever, varied from one to nine days, the average being 5⅓ days, and the total average duration of the disease in the patients who recovered being 6 7/9 days, while of the eight control

cases the average duration of six was 10½ days, and in two the temperature continued for a very long period.

The crucial test is the effect of the injections on mortality, and in this we cannot make a brilliant showing, for while of the fifteen injected patients nine recovered and six died, giving a mortality of 40 per cent.; of the fifteen controls eight recovered and seven died, giving a mortality of 47 per cent. Among the six patients injected with pneumococcus serum alone there were four recoveries and two deaths, while the controls showed five recoveries and one death. Of the nine patients injected with the pneumococcus and streptococcus serum five recovered and four died, while of the controls of these there were three recoveries and six deaths. Repeated injections in patients who had showed no reaction from the first injection were equally unsuccessful.

In conclusion, I would say that the serum injections, while apparently affecting favorably the course of the disease in some cases, appears to have no result in others; that in most cases there appears to be a better reaction on the part of the child after injection than before. It was usually followed by some reduction in leukocytosis, and the percentage of the polynuclear leukocytes was also diminished. In these favorably influenced cases there was little spreading of the disease after injection, and in some a fairly rapid resolution.

The injected patients who lived had a much shorter average course than the controls, and the mortality of the injected cases was slightly less than that of the controls.

The pneumococcus serum presents a safe method of attempting to influence the course of pneumonia in children; the addition of antistreptoccoccus serum seems to offer no advantage over the use of the pneumococcus serum alone.

DISCUSSION

DR. NICOLL said that he had had a fairly large experience with the use of pneumococcus serum in the treatment of pneumonia both in children and in adults, and he thought that the conclusions at which Dr. Freeman had arrived were those that all must come to who had had any experience with this serum, namely, a verdict of "not proven." Sometimes good results were obtained and at other times no results whatever. Dr. Freeman used full doses of the serum; there was no use in using 10 or 15 c.c. One should give at least 100 c.c. and personally he believed in giving it in the veins. Dr. Nicoll said he had recently been made somewhat skeptical in regard to the value of the serum by the results of an attempt he had made to immunize diphtheria cases against secondary pneumonia. The number of children was between forty and fifty, 2½ years of age or under, and at the time of their admission to the hospital were free from pneumonia as far as could be

judged by temperature, pulse and respiration. All of these children were intubated either before admission or soon after so that the reliability of the physical signs in the chest was not great. They were each given 20 c.c. of one-half pneumococcus serum and one-half streptococcus serum. By comparing the death rate from pneumonia in this series, it was found that the results were not remarkably better than those which had been obtained in each of the two previous years and during the same seasons of the year among the same class of cases not so immunized. It was difficult, therefore, to have a great deal of faith in the curative value of a serum which had so little apparent protective power against the organism whose activities it was designed to control. In the last series of cases reported from Germany the serum had been given intravenously in doses impossible to determine, as the method of standardization was not stated and the dosage was regulated according to that method. The results were by no means convincing. In view of the fact that not infrequently good results seemed to follow the use of the serum, he believed that it should be given in prolonged and severe cases of pneumonia which seemed to be daily losing ground, but the dosage should be large. He had not seen any bad effects which could be definitely attributed to the use of the serum, even when given intravenously in large doses. A dose of 100 c.c. given subcutaneously, while it caused a formidable tumor occasioned very little pain and was easily administered with a suitable apparatus.

DR. SOUTHWORTH asked Dr. Freeman if he had used more than one injection of the serum.

DR. FREEMAN replied that he had used a second injection in several cases and none of them did any better after the second than they did after the first injection.

DR. HAND said he had had a limited experience with the use of the serum. He began to use it eleven years ago and the first two cases gave him beautiful results and it seemed to him that he had a specific which was absolute. It lowered the temperature gradually and brought it down to the normal in a few days, although in the first case an empyema did develop. In the second case the serum acted in the same specific way, bringing the temperature down in two days step by step. Then he had three failures with it. Therefore, it seemed to work well in some cases and not in others. Bacteriologists claimed that the pneumococcus, like the streptococcus, was made up of a group of germs and was not an individual germ. If an acute pneumonia in a given case had the same strain one might get better results. The serum might be more bacteriolytic rather than bactericidal and this might account for the failures.

DR. THOMAS MCCLEAVE, Berkeley, Cal. (guest), said that a short time ago he was talking with the bacteriologist of one of the large manufacturing companies, and asking about the antipneumococcus serum; he was informed that the firm had discontinued its manufacture because the reports of its use were so unfavorable they thought it was no longer worth while manufacturing it or using it.

THE WASSERMANN REACTION IN INFANTS AND CHILDREN: A CLINICAL STUDY*

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The diagnosis of early congenital syphilis as a rule is not difficult. The diagnosis of the same disease in later childhood is often a matter of great difficulty. Careful inquiry into the history, both family and personal, may throw no light on the case, and the characteristic signs which would enable one to make a diagnosis may be slight, or entirely absent; yet, later, perhaps at the age of puberty, such signs do arise and the diagnosis is evident. Undoubtedly such cases are syphilitic from the onset, but run a "latent" course, perhaps for several years, and then under certain conditions break out in a more pronounced form.

The diagnosis being thus at times difficult, any measures leading to ease and certainty of detection are eagerly welcomed. Studies of recent years have given us three such measures: the detection of the *Spirochaeta pallida* in the secretions or tissues of the body, inoculation experiments on monkeys or rabbits, the serum reaction of Wassermann. While the clinical diagnosis will continue to be the most important method in the future, as it has been in the past, these other recent methods will be of great value especially in obscure, latent cases. Of these methods the serum reaction is the most widely used and of the greatest practical value. This method depends on the complement-uniting reaction first described by Bordet and Gengou in 1901. In 1905 Wassermann applied this reaction to the diagnosis of syphilis.

"The reaction depends on the fact that serum from a positive syphilitic patient contains certain reaction bodies or antibodies which, in the presence of a known antigen from the liver of a syphilitic fetus, combines with the complement. The complement being bound in this first step, does not enter into combination with the hemolytic system, which is the indicator in the reaction, and therefore hemolysis is prevented, or inhibition of hemolysis occurs, giving a positive reaction. If the serum of a normal person is brought into combination with a known syphilitic

*From the Children's Memorial Hospital.

antigen, derived in the same way as above, there is no union with the complement, which consequently is left free to unite with the hemolytic system, the indicator again, and hemolysis does occur, giving a negative reaction."

In most of the tests made in this series, the Noguchi modification of the Wassermann method has been used. It is not the intention of this paper to enter into a discussion of the relative merits of Wassermann's original method and Noguchi's modification thereof. The evidence seems conclusive, to a clinician at least, that the Noguchi method is fully as reliable as, and perhaps more sensitive than, the Wassermann technic, and yet in the hands of an expert is not too sensitive, i. e., does not give positive results in non-syphilitic cases (Kaliski). It furthermore has the advantage of requiring less blood, a factor of no little importance in carrying out the technic in small children.

TECHNIC

The various steps are as follows: The blood may be obtained from either a vein or, preferably, from a finger or the great toe; only about 1 c.c. is required; to obtain this a finger or the great toe is punctured with a Hagedorn needle, the part massaged toward the puncture and the blood collected in a Wright capsule (Fig. 1). "The straight empty end of the tube is now sealed with a flame, cooled, shaken to drive the blood from the bent end to the straight sealed end, and the bent end is then sealed in the flame. Care must be taken not to apply the heat to the blood itself. After sealing, the tube may be mailed to the serologist for examination. Wright's capsules may be made by drawing out ordinary thin glass tubing in the flame of an alcohol lamp or Bunsen burner.

"The blood-clot and the serum separate in a few hours at room temperature. If the test is not made within two or three days, the serum should be drawn off with a capillary pipet; otherwise, if left in contact with the clot, it will become tinged with the hemoglobin and this will somewhat interfere with the accurate reading of the test" [1] (Fig. 2).

The spinal fluid may be used for the test in cases in which a lumbar puncture is done for either diagnostic or therapeutic purposes, or in certain cases of emaciated, atrophic infants where it seems impossible to obtain enough blood and where a test is imperative; in the latter class of patients a lumbar puncture may be done especially for this purpose.

1. Noguchi: Serum Diagnosis of Syphilis, ed. 2, 1911, p. 54. Lippincott Co., Philadadelphia.

It must be borne in mind, however, that in a small proportion of cases, the spinal fluid will give a negative reaction, when the blood gives a positive one.

DIAGNOSTIC VALUE OF SERUM TEST

The Wassermann test has now been applied to thousands of cases of undoubted syphilis in adults, has been found present in from 60 to 100 per cent. of the cases, according to the stage of the disease, and is universally accepted as of great diagnostic value. The test has also been applied to syphilitic infants and children, though in smaller numbers, and among them also is regarded of great diagnostic significance. Various observers —Mulzer and Michaelis, Bauer, Halberstaedter, Muller and Reiche, Reinhart, Stroscher and others—applying the test to cases of manifest, undoubted syphilis, find it positive in from 96 to 100 per cent. of the cases. There can be no doubt of its diagnostic value then in early as well as in later life.

But most of these observations have been made on cases of undoubted syphilis, cases in which the clinical signs left no doubt of the nature of the disease. Those making the observation have been engaged in "testing" the test, to see if it would "ring true;" to see if it would coincide with the clinical picture of well known, easily recognized cases of the disease. They have proved beyond a doubt that the test does "ring true," that it does react positively in practically all cases with manifest signs of early congenital syphilis—"snuffles," skin lesions, mucous membrane lesions, etc. Indeed, in the very early cases, the reaction is apt to run closely hand-in-hand with the clinical signs; thus Mulzer and Michaelis report cases with suspicious family records, but themselves without physical signs, who gave soon after birth a negative serum reaction, and later, just before, or coincidently with, the breaking out of characteristic signs, a postive reaction.

The use of the test, however, in other groups of cases, those of the obscure or latent type, as a valuable aid in determining the presence or absence of a syphilitic taint, has been little practiced. Comparatively few applications of the test have been made to cases which might be syphilis, yet are without sufficiently well-defined physicial signs to warrant a positive diagnosis. One finds but few large series of these indefinite cases. Isolated examples of this or that condition are reported with either a positive or negative reaction, but not in sufficient number in a particular condition, e. g., arthritis, to justify conclusions as to the frequency of syphilis as a foundation cause of that condition.

Certain affections of the nervous system, however, have been studied with the test. Thus Knopfelmacher and Schwalbe, studying the Wassermann reaction in hydrocephalus, collected twenty-nine cases, eight of which were positive (27 per cent.). They also quote some Danish workers who, among 2,000 cases of mental deficiency, practically all adults, found thirty-one giving a positive reaction. This series included 259 epileptics, only one of whom was positive.

Dean tested 330 cases, children or young adults, in a Potsdam asylum, and found positive results in fifty-one (15 per cent.). The most of these were idiots; they formed the bulk of the positive cases, forty-four of the fifty-one being in this class of patients. He also brings out the significant facts that of the fifty-one positive cases, only nine were clinically syphilis, four were suspected cases, and thirty-seven were entirely without signs of the taint. Furthermore, he found that the proportion of positive cases diminished rapidly after 16 years of age, and suggests that a large percentage of positive results might be obtained in younger children. Dean quotes various authors, Ravait, Brenton, Petit and Gayetoe, who have studied similar cases and have found from 9 to 30 per cent. giving a positive reaction.

Cases illustrating other conditions have been tested in but small numbers. They serve only to emphasize the fact that "symptomless" infants and children may give a positive reaction. Such are mostly very young infants, the offspring of parents known to be syphilitic; e. g., the cases already cited (Mulzer and Michaelis), also cases mentioned by Hochsinger: infants in whom the physician has reason to suspect a syphilitic inheritance and therefore has performed the serum test.

FIELD OF APPLICATION

There is a wide field for the use of the Wassermann serum test, as yet but little explored, in that class of patients frequenting our dispensaries and hospital wards. No extensive investigations of the serum test on a broad and comprehensive scale have yet been carried on among these patients. We are all familiar with the type: anemic, undersized, with lymph-nodes generally enlarged, often with a high lymphocyte count, they are generally below par, perhaps degenerate, and present a condition due to a great variety of causes, one of which *may* be syphilis. It is in this type of cases especially that the Wassermann test may be of great

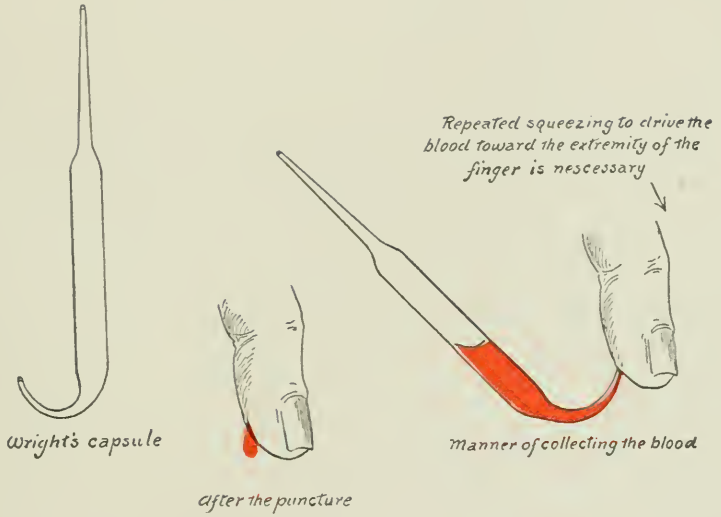

Fig. 1.—Method of collecting blood from the finger-tip by means of a Wright capsule. (From Noguchi: The Serum Diagnosis of Syphilis, 1912.)

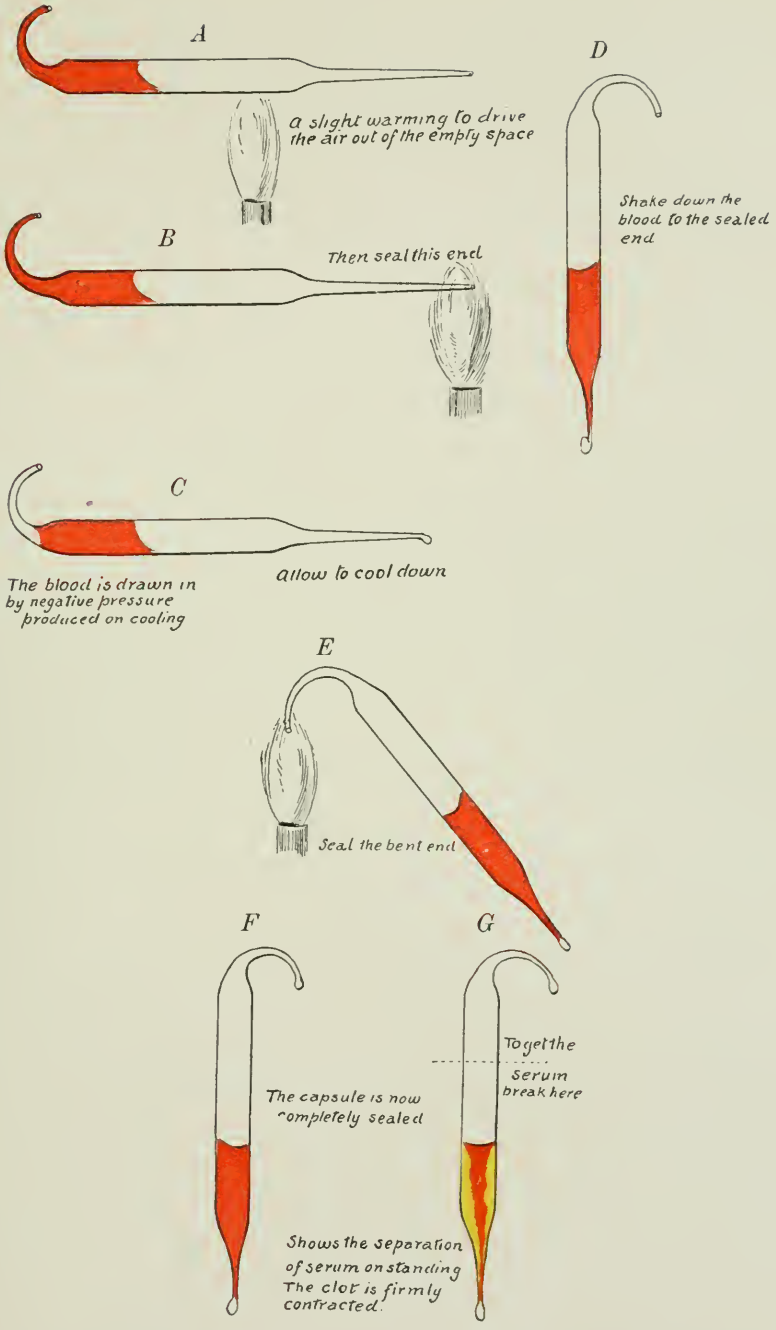

Fig. 2.—Showing the further steps in the technic of collecting the blood and obtaining the serum in the serum test for syphilis. (From Noguchi: The Serum Diagnosis of Syphilis, 1912.)

value, for its presence in such children is very strong evidence pointing toward a syphilitic foundation for their deteriorated, degenerate condition; its absence almost certain proof that syphilis does not exist.

OBJECTS OF THE PRESENT STUDY

It is with this class of children that this paper deals. The present study has been undertaken to determine, as far as possible, the following points:

1. What proportion of our hospital children will show a positive serum reaction?

2. What proportion of the positive cases present signs suggestive of syphilis?

3. Does a positive serum reaction in a child without characteristic physical signs mean syphilis?

The tests in the present series were made by Drs. W. E. Post, J. F. Waugh and H. K. Nicoll, and I wish to express my deep appreciation for the courtesy and skill of these gentlemen in thus making the work possible. Though not connected with the Hospital, they have given freely of their time and thought purely from "love of the cause" and interest in an investigation which they as well as myself believe to be worth while, indeed even necessary. The work would have been impossible without their generous cooperation.

Tests were made on 102 infants and children, on six mothers and two fathers. On the children, 111 tests in all were made, twenty-eight Wassermann, eighty-three Noguchi. The blood was used in ninety cases, the spinal fluid in twelve cases. The children ranged in age from 3 days to 12 years; all, with but two exceptions, were patients at the Children's Memorial Hospital. There were thirty-nine positive reactions, sixty-two negative, and one case with a positive Noguchi but negative Wassermann. Thus 38 per cent. of the cases gave a positive reaction.

The mothers of the children in four positive cases were tested and gave one negative and three positive reactions; the one with the negative reaction had had the last one of three miscarriages two years before the test was made; she had had no specific treatment. The mothers of two negative-reacting children both gave negative results. Of the two fathers, one, with a positive-reacting child, himself gave a positive result. The second father was the parent of the 18-months-old infant with a positive Noguchi and negative Wassermann reaction and gave two negative Wassermanns,

done by two different serologists a few days after the child was tested. No Noguchi was done on the father.

None of the 100 children entered the hospital as a case of syphilis. The admissions diagnoses are given in Table 1.

We note the great variety of diseases represented, involving practically all of the different systems of the body: nervous, circulatory, bony, respiratory, etc. But the affections which most attract attention by their positive results are those involving the nervous and circulatory systems, and the tuberculous infections. There are seventeen cases presenting diseases of the nervous system, with nine positive and eight negative reactions; sixteen cases of heart trouble, with seven positive and nine negative, and twenty-six tuberculous cases, with eight positive and eighteen negative reactions. There are fifteen cases affecting the respiratory system, five positive and ten negative. The remainder are scattered among the various conditions represented in Table 1. This table shows the varied character of the cases tested and also the proportion of positive cases. The number of cases, however, in a given condition is so small that the percentage of positive cases in such given condition cannot be considered as by means an average percentage; this can be determined only by future investigations when large numbers of cases have been tested and analyzed.

Our chief interest of course is in the positive cases. These will now be considered in groups by themselves.

POSITIVE CASES

The total number of cases giving a positive reaction is thirty-nine, ranging in age from 1 to 12 years, distributed as follows:

Age, Years	No. of Cases	Age, Years	No. of Cases
Under 1	5	7	4
Between 1 and 2	4	8	3
2	1	9	4
3	4	10	2
4	4	11	3
5	2	12	2
6	1		

There were twenty-five boys and fourteen girls.

METHOD OF STUDY

The cases have been studied from the following points of view: the admission diagnosis, the family history, the patient's own previous record of development and general health, the physical condition at the time of

TABLE 1.—GIVING A SYNOPSIS OF ADMISSION DIAGNOSIS AND REACTIONS IN ALL CASES

Admission Diagnosis	Totals	Positive	Negative	Per cent. Positive
Tuberculosis—				
General	3	2	1	..
Meningeal	4	1	3	..
Pulmonary	2	1	1	..
Joints	17	4	13	31
	26	8	18	
Nervous System—				
Brain tumor	1	1	0	..
Little's disease	3	1	2	..
Encephalocele	1	0	1	..
Meningitis (meningococcus)	1	0	1	..
Meningitis, chronic	1	0	1	..
Microcephalus	1	1	0	..
Amaurotic family idiocy	1	1	0	..
Epilepsy	4	2	2	..
Spinal cord lesion	1	1	0	..
Poliomyeloencephalitis	2	1	1	..
Miscellaneous	1	1	0	..
	17	9	8	
Circulatory System—				
Congenital heart	5	2	3	40
Chronic endocarditis	11	5	6	45
	16	7	9	
Respiratory System—				
Rhinitis	1	1	0	..
Tonsils and adenoids	8	3	5	37
Bronchitis	1	0	1	..
Pneumonia	4	1	3	..
Asthma	1	0	1	..
	15	5	10	
Digestive System—				
Hare-lip	5	1	4	20
Enteritis	5	1	4	20
	10	2	8	
Osseous System—				
Arthritis periostitis	1	1	0	..
Osteomyelitis	1	1	0	..
Club-foot	2	0	2	..
Fractured toe	1	0	1	..
	5	2	3	
Miscellaneous—				
Anemia	2	1	1	..
Keratitis	3	2	1	..
Phimosis	1	1	0	..
Rachitis	5	1	4	20
Still's Disease	1	1	0	..
Typhoid fever	1	0	1	..
	13	6	7	
Totals	102	39	63	38

TABLE 2.—ADMISSION DIAGNOSIS IN THE POSITIVE CASES

	No. of Cases
Tuberculosis—	
General	2
Joints	4
Meningeal	1
Pulmonary	1
Total	8
Nervous System—	
Brain tumor	1
Little's disease	1
Microcephalus	1
Amaurotic family idiocy	1
Epilepsy	2
Spinal cord, lesion of?	1
Poliomyeloencephalitis	1
Miscellaneous nervous	1
Total	9
Respiratory System—	
Rhinitis	1
Tonsils and adenoids	3
Pneumonia	1
Total	5
Circulatory System—	
Congenital heart	2
Chronic endocarditis	5
Total	7
Osseous System—	
Periostitis	1
Osteomyelitis	1
Total	2
Digestive System—	
Hare-lip, etc.	1
Enteritis	1
Total	2
Miscellaneous—	
Anemia	1
Keratitis	2
Phimosis	1
Rachitis	1
Still's disease	1
Total	6
Grand Total	39

making the test, and, in the fatal cases, the results of autopsy. Information along these lines seemed necessary in order to "check up" the test and to answer the second and third questions. Details of the cases are given in Table 3.

The admission diagnoses are given in Table 2. Study of this table shows that of the thirty-nine positive reactions, eight were obtained in tuberculous trouble, nine in affections of the nervous system, five respiratory, seven circulatory, two osseous, two digestive, and six were in miscellaneous conditions.

The family history was investigated with special reference to syphilis. It shows a positive record of this disease in four cases, a suggestive record in sixteen cases, a negative one in eighteen cases, no history obtainable in two cases. By a "positive" record is meant a definite history of clinical syphilis in another member of the family or a positive Wassermann reaction in either parent; by a "suggestive" record is meant a history of miscarriage in the mother, of serious mental or nervous trouble in another member of the family, or the occurrence of a positive reaction in a brother or sister not of adult age. Thus, of the thirty-nine cases twenty-one (56 per cent.) show a family history conclusive or suggestive, of a syphilitic taint. Only 20 per cent. of the negative cases show such family history.

The family history is often such an important factor in arriving at a diagnosis of congenital syphilis, that it has seemed worth while thus to consider it by itself with reference to the serum reaction in the positive cases. But the personal record and the physical condition of the child himself must, after all, finally determine the question. The cases, therefore, have been studied with reference to the combination of all three of these factors, i. e., family history, personal record and physical examination, in order to see to what extent these factors and the serum reaction coincide. For this purpose they will now be rearranged in five separate groups.

Group I.—Cases with family history, personal record and physical signs, all suggestive, or even diagnostic, of syphilis. There are nine of these cases.

Group II.—Cases with either family or personal history, plus physical signs, suggestive of syphilis. There are nine of these cases.

Group III.—Cases with only physical signs suggestive of syphilis. There are six of these cases.

Group IV.—Cases with either a suggestive family history alone, or a suggestive personal record alone. There are five of these cases.

Group V.—Cases without either family history, personal record or physical signs suggestive of syphilis. There are ten of these cases.

The cases of Groups I, II and III may all be regarded as clinically syphilis. All of these, twenty-four in number, or 63 per cent. of the positive cases, give suggestive physical signs. Among the negative cases only 5 per cent. give such suggestive signs. Cases of Group IV, in view of either a positive family history or positive personal record plus a positive serum reaction, are probably syphilitic, making in all, twenty-nine cases, or 28 per cent. of the whole series, which are probably syphilis.

Group V is an important group and requires special discussion, but before proceeding with that discussion, certain cases in the other groups are of interest.

GROUP I.—Cases 26 and 27 were twin brothers who entered the hospital for the removal of tonsils and adenoids. Both were undersized though of different weights; each had a goiter. The mother had had three miscarriages since the birth of the twins but gave, at this time, a negative Noguchi reaction. The twins were put on mercurial treatment, Nov. 11, 1911, and began to improve immediately, the more vigorous one faster than his brother; the former went from 52½ pounds, Feb. 16, 1912, up to 54½ pounds, March 23, 1912, and on the latter date had a negative reaction; his brother, between the same dates, went from 50 pounds to 51½ pounds and still gave a positive reaction. The more vigorous one of these twins thus gave evidence of greater resistance to his hereditary taint, not only by the improvement in his general physical condition, but by the change of his positive reaction into a negative one.

Cases 35 and 36 were also brothers, instances, again, of "familial" syphilis, each showing a keratitis, one also an arthritis and one also deafness. Both left the hospital unimproved after three weeks' treatment with mercurials; five months later the arthritis one returned with his keratitis much worse and his serum reaction still positive. He is now under observation, improving under vigorous mercurial treatment.

GROUP III.—Case 34 was an anemic, 18-months-old infant in private practice; she was backward about her teeth, was fat and "flabby," had a lymphocytosis and a dactylitis. Her blood gave a markedly positive Noguchi reaction. One of the leading syphilographers of Chicago saw her with me in consultation, could not accept the specificity of the Noguchi reaction, doubted the diagnosis of syphilis, and suggested a straight Wassermann test. This was done and was reported negative. Calomel, one-tenth gr. t. i. d. for four days had been given after the Noguchi and before the Wassermann test, but it is improbable that this

small amount of mercury converted a positive into a negative reaction. The tests were done by different serologists, both skilful and expert workers. The father was an educated man, appreciated the importance of the truth, denied syphilis, and his blood gave a negative Wassermann reaction, the test being made by the man who found the negative reaction in the child. No Noguchi was done on the father.

GROUP IV.—Case 3, a 3-year-old child, entered the hospital as a case of tuberculous meningitis. The father gave a history of "soft" chancre seven years before (i. e., four years before the birth of the patient), the mother a history of one miscarriage (date ?); and of a baby younger than the patient who had always been "delicate with heart trouble" and who died at 1 year. The patient's spinal fluid gave a strong Noguchi reaction. The autopsy showed a marked tuberculous meningitis, with tubercle bacilli present in great numbers in the exudate at the base of the brain. There were no lesions of syphilis, either gross or microscopic; no spirochetes in the meningeal exudate examined by the Levaditi method. The head only was examined.

GROUP V.—The cases of this group cannot be regarded as clinically syphilis in the ordinary sense of the term, and such a diagnosis would rest largely on the results of the serum test; in these cases the test was positive. Are we, then, to accept such a result as evidence of the presence of syphilis? Are we to regard as cases of syphilis, patients who, without suspicious family history, without suggestive personal record or physical signs, yet nevertheless give a positive serum reaction? How are we to explain the positive reaction in such patients?

There are three possible explanations:

1. The reaction is correct and is due to some condition other than syphilis.

2. The reaction is correct and is due to syphilis, which may be the real underlying cause of the condition named, or may be a factor predisposing toward some other infection, e. g., tuberculosis.

3. The reaction is incorrect, due to some error of technic.

The first supposition, that the reaction is due to some condition other than syphilis, is untenable. Aside from syphilis, the only conditions in which a positive Wassermann reaction has been found are scarlet fever, jaundice, leprosy, carcinoma, diabetes mellitus and possibly malaria. None of these conditions existed in any of the cases in Group V; furthermore, there is no ground for believing that any of the conditions named

in this group would cause a reaction of such specificity as is the Wassermann reaction.

The second supposition, that the reaction is correct and is due to syphilis, the physical conditions found being either unusual manifestations of syphilis or coexisting as separate entities, e. g., tuberculosis, is debatable.

Syphilis is of course a most protean disease. Not a single tissue of the body is there that may not be attacked by the virus, once the latter has gained access to the body. Its obscurity and latency at times are well known. Especially in congenital syphilis may its manifestations be most varied. They may furthermore be latent for a period, giving rise to no symptoms or signs, yet later showing characteristic stigmata of the disease, the so-called *syphilis hereditaria tarda*. It is conceivable that the cases in Group V may belong to this class; that they are cases of latent, late syphilis and that they may show active signs of the disease later on in life, perhaps at puberty. Before the advent of the serum test it would not have occurred to any clinician examining these patients to regard them as syphilitic. He would have classified them as above, and their anemia, lymphocytosis, adenitis and general deterioration he would have attributed to general causes — bad hygiene, bad food, lack of care, etc. But among the causes to which these conditions *may* be due is the specific cause syphilis; hence, finding these conditions present, finding also present a test so strongly diagnostic of syphilis as is the serum test it is entirely possible that these cases in Group V may be syphilitic, that they are in reality cases of hereditary syphilis, in a latent stage; cases in which the disease process is so sluggish that it has as yet given rise to no gross, evident sign characteristic of the taint, yet active enough to produce a more or less deteriorated condition and a positive result when tested by the delicate serum reaction.

This reasoning, however, cannot, I believe, apply to the three fatal cases in the group, Cases 12, 31 and 38. Cases 31 and 38 came to autopsy and showed no signs gross or microscopic of syphilis. No spirochetes were detected in the liver in either case. The heart muscle was not examined for the spirochetes, and it is possible, in view of recent investigations, notably by Warthin, that they might have been found in the tissues of that organ. The third fatal case, Case 12, was one of amaurotic family idiocy; it gave a negative reaction, June 26, 1910, a positive one six months later, Jan. 22, 1911, both tests being made by the same serologist. No autopsy was obtained, but the autopsies which have been made

on cases of this disease do not mention syphilitic changes in the tissues. Syphilis seems improbable in our case. Noguchi,[1] page 134, alludes to one case of amaurotic family idiocy with a negative reaction.

Case 1 must also be questioned. No definite diagnosis was made. The patient was a 3-year-old child who came in after a three weeks' illness with typhoidal symptoms; Widal reaction, blood culture and Pirquet test were all negative. It was probably a case of miliary tuberculosis.

The patient was taken out of the hospital after a week's stay and nothing further was heard of him. There was nothing about him to suggest syphilis.

Concerning the other cases of the group, there is possibly more ground for considering them as syphilitic; five of them involve disease of the osseous system: two of joint trouble thought to be tuberculous, a chronic osteomyelitis, a case of Still's disease, one of Little's disease with bony changes thought to be rachitic. The tendency of the syphilitic virus to attack the bony tissues is well known, and syphilis cannot with certainty be excluded in any of these cases. Clinical observations and serum tests of the future must determine how frequently these bone affections are due to luetic infection.

The case of endocarditis included in this group is interesting: it showed a reaction at first "doubtful," a week later "faintly positive," and a month later "positive;" in view of these reactions and of the frequency with which the other cases of endocarditis of this series, cases with suggestive or characteristic signs of syphilis, have shown positive reactions, there is probably little doubt of the basic nature of this case, little doubt that it is syphilis. But as the case illustrates a condition "on trial," as it were, in this paper, and presented none of the signs regarded in the past as suggestive of syphilis, it must be classified, for the present, at least, in this group. Studies of the future may or may not show that endocardial affections are of such frequent occurrence in congenital syphilis that their presence is suggestive of the disease and must always arouse a suspicion of its existence.

The third supposition, that the reaction is incorrect and is due to some error in technic, must be considered. Such an error might arise from (1) change in the blood after taking and before testing, or from (2) some imperfection in one of the substances or reagents used. Due care was used in the handling of the blood, keeping it at a proper temperature, etc. It is of course possible that hemolysis may have taken place before testing and thus at the test hemolysis was prevented and a positive

TABLE 3.—CASES SHOWING POSITIVE SERUM REACTION

Case No.	Age, Years	Sex	Admission Diagnosis	Family History	Previous History	Examination	Reaction	Remarks
1	3	M	Miliary Tuberculosis?	Uncle died of phthisis	Always delicate; typhoid symptoms 3 weeks.	Emaciation; glands +; spleen +; T. 98-104 F.; blood culture neg. Widal negative.	Noguchi +	Pirquet negative left in 1 wk:; unimproved.
2	12	M	General debility Tb.? 11/14/10	Mother had 3 or 4 miscarriages; 7 other children well.	Developm't backward; dull mentally; pneumonia 4 years ago; scarlet fever 2 years ago; measles 2 years ago.	Poor development; glands +.	Noguchi + 11/26/10	Pirquet + 11/26/10
3	3	M	Tb. Meningitis 4/4/12	Father had "soft chancre" 7 years before; mother had one miscar.; younger brother died one year ago of "heart trouble"; always delicate.	Gen. development normal; present illness began 7 weeks ago.	Typical meningeal signs; Sp. Fl. clear; lymphocytes; Tb. bacilli? Pirquet negat. Double otitis media.	Sp. Fl. Noguchi +++	Died 4/8/12. Autopsy (on head only) showed tb. meningitis, bacilli in exudate at base of brain; no syphilitic changes.
4	1½	F	Broncho-Pneumonia Tb.?	Mother had one miscarriage before birth of patient.	Devel'pm't poor; cough for 3 weeks.	Nutrition poor; color waxy; nasal discharge; nose flat; glands+; bronchitis; consolidation ? tonsils +; spleen +.	+	Pirquet ++

5	7	M	Tb. Hip	Negative	Measles 1 yr. ago; pertussis; date ? Fall 3 weeks ago; R. hip tender since; lame.	Nutrition good; glands +; teeth irreg. and notched; R. hip tender.	Noguchi +	Pirquet negative
6	4	F	Tb. Knee	Negative	Development normal; knee symptoms 3 mos.	Pale, nutrition fair; tonsils +.	Wassermann +	Pirquet ++
7	5	F	Tb. Spine 7/15/10	Negative	Pertussis at 1 year; present trouble began 1½ years ago.	Spinal deformity; glds. +; consolidation R. lung, post. an 1/6/11.	Noguchi + 2/1/11	.....
8	4	M	Tb. Spine 5/5/11	?	Measles 1 yr. ago and since, pain in back and can not walk.	Pale, nutrition poor. Chest: enlarged bronchial glands ? Abdomen: Tb.? nodules; spleen +; liver +; choked disks (1/20/12, 2/21/12); T. 97-102 F.	Wassermann + 2/24/12	Has had tuberculin regularly since admission to date.
9	11	M	Papillitis 1/17/11 Intracranial tumor.	Negative	Good till 2 years ago; since, sick headaches.	Nutrition fair; general incoördination; ataxic gait; paralysis of L. abducens; choked disk R.	Noguchi + 2/2/11	Died 2/10/11. Autopsy showed tumor of L. cerebellum. No signs of syphilis anywhere.
10	3	M	Little's disease	?	Always delicate, measles, date ? meningeal symptoms for 2 wks.	Nutrition poor; rigidities; glands +; rickets signs.	Noguchi + 9/5/10 Noguchi + 1/19/11	Pneumonia 1/13/11 Antitoxin
11	7	F	Microcephalus 1/9/11	Mother had one still-born, one abortion, then the patient and since two still-born.	Backward. Pneumonia at 2 years.	Nutrition poor; physical and mental development backward; tonsils+; head small.	Noguchi + 1/11/11	.....

TABLE 3.—CONTINUED

Case No.	Years Age.	Sex	Admission Diagnosis	Family History	Previous History	Examination	Reaction	Remarks
12	4	M	Amaurotic family idiocy 6/24/10	Negative	Always delicate; at 1 week vomiting and convulsions.	Emaciation; eyes show characteristic ch'ges; glands +.	Noguchi — 6/26/10 Noguchi + 1/22/11	Death 9/8/11
13	4	F	Epilepsy 2/24/11	Alcoholism, insanity, migraine and cancer in grandparents. Father had "soft chancre" one year before marriage. Mother had 1 child healthy, then miscarriage, then patient.	Measles and pertussis in infancy; diphtheria 2 years ago; characteristic seizures since 7-8 mos. old.	Parietal bosses +; nose flattened; tonsils +; glands +.	Noguchi ++ 2/27/11	.....
14	8	M	Epilepsy 3/18/11	Epilepsy in maternal G. M. Mother had petit mal? 3 other children well.	Labor instrumental; mentally slow; measles and scarlet fever 4 yrs. ago; varicella 2 mos. ago; pneumonia 3 mos. ago; "spells" for 2 years.	Head asymmetrical; otitis; pigeon-breast.	Noguchi + 3/9/11	.....
15	10	F	Lesion of spinal cord 9/30/10	Negative	Weak at birth; measles at 7 years; varicella at 9 years; fall 1 yr. ago; since spinal symptoms.	Nutrition poor; parcsis R. limbs; teeth notched; glands +; patellar ++; tonsils and adenoids removed; no spirochetes found.	Noguchi + 10/5/10	.....

16	11	F	Poliomyeloencephalitis	Negative	Pneumonia; date ? Typhoid date ? Unable to walk for 2 yrs.	Teeth notched and decayed; tonsils +; spastic lower limbs.	Noguchi + 2/9/11	.....
17	3	M	Backward speech 12/17/10	Father had chancre; autopsy showed syphilis. Died 8 mos. ago. Mother's blood shows pos. Noguchi; younger brother has neg. Noguchi. Paternal g. f. had syphilis?	Developm't slow; bronchopneumonia at 2½ years.	Nervous, pale; development poor; can't talk; liver +.	Noguchi + 12/19/10	Pirquet ++
18	½	M	Congenital heart disease 1/4/11	Mother had miscarriage 5 years ago; 3 other child'n healthy; mother died 1 week ago of pneumonia and endocarditis.	Full term, instruments, condition good. Pertussis 3 mos. ago followed by pneumonia. Double otitis, 1 mo.	Nutrition poor; organic heart-signs; ears discharging; weight 10 lbs., 2 oz.	Noguchi + 2/9/11	Left 7/3/11 Mercury from 2/28/11 to 4/6/11
	1¼		10/27/11	.....	.....	Reentered in collapse	.....	Blood and Sp. Fl. from autopsy negative, by both Wassermann and Noguchi. No syphilitic changes in tissues
19	1½	M	Congenital heart disease 11/8/10	Paternal G. F. died of heart trouble; mother had one miscarriage at 7 mos; 1 other child 2 years old healthy. Mother's blood gives positive Noguchi 12/28/10.	Always delicate.	Developm't and nutrition poor; bronchopneumonia; organic heart murmur; spleen +; liver ++.	Noguchi + 12/1/10	Recovery from pneumonia. Died July, 1911, at home.

TABLE 3.—CONTINUED

Case No.	Age, Years	Sex	Admission Diagnosis	Family History	Previous History	Examination	Reaction	Remarks
20	8	M	Endo-pericarditis 3/15/11	Father died phthisis, 2 years ago.	Weak since 5 yrs. old; measles and diphtheria; rheumatism 1 yr. ago; for 1 mo. cough, pain in chest, weakness, dyspnea.	Pale, nutrition fair; tonsils +, glands +. Endopericarditis.	Noguchi Doubtful—3/29/11 Weakly+4/6/11 Positive 5/11/11	.....
21	6	F	Endocarditis, mitral aortic? 9/10/11	Father has Noguchi +++ on 3/7/12	Measles; repeated tonsillitis; joint pains recently.	Pale, nutrition poor; glands +, tonsils +; nose flat, teeth bad and irregular; mitral murmurs, aortic murmurs. ?	Wassermann + 2/13/12	Pirquet +++
22	10	F	Endocarditis, mitral aortic? 11/22/10	Mother has goiter; two children died at birth. Mother's blood shows Noguchi ++.	Backward; measles and pertussis at 2 years; mumps at 5 yrs. Tonsillitis at 4 and 7 yrs. Scarlet fever 5 mos. ago, followed by polyartic. rheumatism. Blood and albumin in urine 2 mos. ago.	Nutrition poor; pale; tonsils +; teeth notched; mitral murmurs; aortic murmurs; acute nephritis.	Noguchi + 12/15/10	Died 4/9/11
23	9	M	Endocarditis	Four older children healthy; then 2 miscarriages just before birth of patient. Not preg. since patient.	Development normal; chorea 3 mos. ago; edema for 3 weeks.	Nutrition good; tonsils ++; teeth irregular, notched; mitral murmur; glands +; liver +; no spleen.	Noguchi + (weak)	.....

24	7	F	Endopericarditis 7/21/11	Mother had 2 miscarriages; poor health since last baby, five years ago.	Measles at 11 mos.; scarlet fever at 4 yrs. Sore throat frequently; for 3 weeks abdominal pain.	Nutrition poor; pale; tonsils +; pericarditis; mitral murmur.	Noguchi + 8/6/11	.....
25	¼	F	Rhinitis—"snuffles" 1/16/10	Another child died at 5 weeks of a bad "cold."	Normal at birth; "snuffles" for 2 weeks.	Nutrition fair; glands +; bronchitis, nasal discharge; no spirochetes found; spleen +.	Sp. Fl. Noguchi + 4/29/10	Left improved 7/17/10
26	9	M	Tonsils and adenoids	Mother had miscarriages 1½ yr., 4 yrs. and 7 yrs. after birth of twin patients.	Developm't backward; pertussis and mumps at 18 mos.; measles at 5 yrs.; recurrent tonsillitis.	Development and nutrition poor; pale; tonsils +; thyroid ½; glands +.	Noguchi + 11/9/11 Noguchi + 12/20/11 Noguchi + 2/26/12 Noguchi + 3/23/12	.....
27	9	M	Tonsils and adenoids	Mother: Noguchi negative. Twin brother of Case 26.	As in brother	As in brother; thyroid +, etc., but is more vigorous and 2 lbs. heavier. Both received Hg. from 11/9/11 to 3/23/12.	Noguchi + 11/9/11 Noguchi + 12/20/11 Noguchi + 2/26/12 Noguchi + 3/23/12	.....
28	4	M	Tonsils and adenoids	First 4 pregnancies miscarried at 8 mos.; then 5 living children.	Measles, date ? Varicella, date ? Repeated sore throat; adenoid symptoms.	Developm't poor; pale; tonsils +; nose flat; rachitic signs; albuminuria.	Noguchi + 3/5/12	.....
29	2	M	Lobar pneumonia	Negative	Pneumonia at 1 year.	Nutrition poor; pale; nose flat; vacant stare and "grin"; tonsils+.	Wassermann + 2/19/12	Pirquet negative 2/19/12

TABLE 3.—CONTINUED

Case No.	Age, Years	Sex	Admission Diagnosis	Family History	Previous History	Examination	Reaction	Remarks
30	17*	M	Hare-lip, cleft palate 12/28/10	First child still-born; 3 others living, well; patient is fifth child.	Full term; condition fair.	Condition fair; hare-lip and cleft palate.	Noguchi + Sp. Fluid 1/11/11	Operation 5/22/11 Died 5/23/11
31	1/6	M	Enterocolitis, Convulsions	Negative.	Well at birth; "cold" for 10 days; convulsions for 24 hours.	Emaciation, pallor; moribund. Sp. Fl. neg. for bacteria; Sp. Fl. pos. for Noguchi.	Blood post-mortem gave positive Noguchi	Autopsy 10 hrs. after death; no signs of syphilis.
32	11	F	Fracture of ulna 10/30/10	Mother died insane 5 years ago.	?	Pale; "saddle" nose; teeth irregular, notched; glands +; old scars on both shins. Fracture of L. ulna; *x*-ray shows multiple periostitis in both upper limbs.	Noguchi + 12/6/10	Discharged 1/27/11 Improved on Hg.
33	7	M	Osteomyelitis 3/27/10 Readmitted 12/7/10	Negative	Measles at 1½ years; scarlet fever at 3½ years; for 7 mos. pain in legs, fever, sweating.	Nutrition fair; both tibiae have discharging sinuses. As above.	Noguchi + 12/20/10	Disch'd 9/10/10 improved Given Hg and KI improved.
34	1½	F	Anemia	Negative. Father had 2 negative Wassermanns.	Normal development. For 3 weeks daily rise of temperature; cause ?	Pale; nose flat; tonsils +; dactylitis.	Noguchi + 1/7/11 Wassermann — 1/17/11	Calomel. Tests by different men.

35	9	M	Keratitis, tonsils and adenoids 9/13/10	Mother had no miscarriages. Brother Case 36.	Developm't normal till 5 yrs., then pertussis and since deafness and eye trouble. No ear discharge. Mumps at 3 yrs.; varicella at 4 yrs.; scarlet fever 5 mos. ago; diphtheria 5 mos. ago; "Lung-fever" at 2 yrs.; repeated tonsillitis.	Dull. Glands +; tonsils and adenoids; keratitis; deafness; no discharge from ears; nasal discharge.	Noguchi + 9/22/10	.....
36	8	M	Arthritis and keratitis, 8/14/10 Re-entered 3/12/12	See Case 35 (Brother).	Bronchitis in infancy; tonsillitis often; jaundice 3 mos. ago; joints swollen and tender since.	Developm't and nutrition poor; pale; tonsils and adenoids; glands +; keratitis; knee swollen.	Noguchi positive 9/29/10 after 1 month of Hg. treatment. Wassermann — Noguchi + 3/15/12	Discharged 10/8/10 No treatment since discharge.
37	12	M	Phimosis	Patient oldest child; 3 miscarriages since; 6 other children, well. Twins 2 years ago born with deformed chest. Father had "sores" when first married.	Born at 7 mos., had no finger nails; was asphyxiated; much eye trouble; measles at 6 years; scarlet fever at 8 years; diphtheria 1 year ago.	Development fair; blepharitis; teeth irregular, in double row; palate high; tonsils +; sternum prominent.	Noguchi + 12/18/11	.....
38	1⅓	M	Rachitis gastro-enteritis 6/29/10	Negative.	Negative.	Developm't and nutrition poor; rachitic signs; spleen +.	Noguchi ++ 11/28/10	Pirquet negative. Died 2/11/11. Autopsy showed no gross nor microscopic signs of syphilis.
39	5	F	Still's disease	Negative.	Measles 3 years ago; pertussis 2 years ago; for 1 year pain in limbs and joints; unable to walk.	Nutrition poor; rachitic changes; swelling and stiffness of joints.	Noguchi + 10/24/10 1/9/11 Noguchi — 1/19/11	Hg and KI from Oct. to March, 1911.

TABLE 4.—CASES IN TABLE 2 GROUPED WITH REFERENCE TO THE RELATION OF FAMILY HISTORY, PERSONAL RECORD AND PHYSICAL EXAMINATION TO THE SERUM TEST. POSITIVE CASES

GROUP I

Case No.	Age, Years	Sex	Admission Diagnosis	Family History	Previous History	Examination	Reaction	Remarks
13	4	F	Epilepsy 2/24/11	Alcoholism, insanity, migraine and cancer in grandparents. Father had "soft chancre" one year before marriage. Mother had 1 child healthy, then miscarriage, then patient.	Measles and pertussis in infancy; diphtheria 2 years ago; characteristic seizures since 7-8 mos. old.	Parietal bosses +; nose flattened; tonsils +; glands +.	Noguchi ++ 2/27/11	.....
11	7	M	Microcephalus 1/9/11	Mother had one stillborn, one abortion, then the patient and since two still-born.	Backward. Pneumonia at 2 years.	Nutrition poor; physical and mental development backward; tonsils+; head small.	Noguchi + 1/11/11	.....
17	3	M	Backward speech 12/17/10	Father had chancre; autopsy showed syphilis. Died 8 mos. ago. Mother's blood shows pos. Noguchi; younger brother has neg. Noguchi. Paternal g. f. had syphilis?	Developm't slow; bronchopneumonia at 2½ years.	Nervous, pale; development poor; can't talk; liver +.	Noguchi + 12/19/10	Pirquet ++
26	9	M	Tonsils and adenoids	Mother had miscarriages 1½ yr., 4 yrs. and 7 yrs. after birth of twin patients.	Developm't backward; pertussis and mumps at 18 mos.; measles at 5 yrs.; recurrent tonsillitis.	Developm't and nutrition poor; pale; tonsils +; thyroid +; glands +.	Noguchi + 11/9/11 Noguchi + 12/20/11 Noguchi + 2/26/12 Noguchi + 3/23/12	.....

27	9	M	Tonsils and adenoids	Mother: Noguchi negative. Twin brother of Case 26.	As in brother.	As in brother; thyroid +, etc., but is more vigorous and 2 lbs. heavier. Both received Hg. from 11/9/11 to 3/23/12.	Noguchi + 11/9/11 Noguchi + 12/20/11 Noguchi + 2/26/12 Noguchi — 3/23/12	.....
35	9	M	Keratitis, tonsils and adenoids 9/13/10	Mother had no miscarriages. Brother Case 36.	Developm't normal till 5 yrs., then pertussis and since deafness and eye trouble. No ear discharge. Mumps at 3 yrs.; varicella at 4 yrs.; scarlet fever 5 mos. ago; diphtheria 5 mos. ago; "Lung-fever" at 2 yrs.; repeated tonsillitis.	Dull. Glands +; tonsils and adenoids; keratitis; deafness; no discharge from ears; nasal discharge.	Noguchi + 9/22/10	.....
36	8	M	Arthritis and keratitis, 8/14/10 Re-entered 3/12/12	See Case 35 (Brother).	Bronchitis in infancy; tonsillitis often; jaundice 3 mos. ago; joints swollen and tender since.	Developm't and nutrition poor; pale; tonsils and adenoids; glands +; keratitis; knee swollen.	Noguchi positive 9/29/10 after 1 month of Hg. treatment. Wassermann — Noguchi + 3/15/12	Discharged 10/8/10 No treatment since discharge.
30	17*	M	Hare-lip, cleft palate 12/28/10	First child still-born; 3 others living, well; patient is fifth child.	Full term; condition fair.	Condition fair; hare-lip and cleft palate.	Noguchi + Sp. Fluid 1/11/11	Operation 5/22/11 Died 5/23/11
37	12	M	Phimosis	Patient oldest child; 3 miscarriages since; 6 other children, well. Twins 2 years ago born with deformed chest. Father had "sores" when first married.	Born at 7 mos., had no finger nails; was asphyxiated; much eye trouble; measles at 6 years; scarlet fever at 8 years; diphtheria 1 year ago.	Development fair; blepharitis; teeth irregular, in double row; palate high; tonsils +; sternum prominent.	Noguchi + 12/18/11	.....

*17 days.

TABLE 4.—CONTINUED

GROUP II

Case No.	Age, Years	Sex	Admission Diagnosis	Family History	Previous History	Examination	Reaction	Remarks
4	1½	F	Broncho-Pneumonia Tb.?	Mother had one miscarriage before birth of patient.	Developm't poor; cough for 3 weeks.	Nutrition poor; color waxy; nasal discharge; nose flat; glands+; bronchitis; consolidation; tonsils +; spleen +.	+	Pirquet ++
9	11	M	Papillitis 1/17/11 Intracranial tumor	Negative	Good till 2 years ago; since, sick headaches.	Nutrition fair; general incoördination; ataxic gait; paralysis of L. abducens; choked disk R.	Noguchi + 2/2/11	Died 2/10/11. Autopsy showed tumor of L. cerebellum. No signs of syphilis anywhere.
21	6	F	Endocarditis, mitral, aortic? 9/10/11	Father has Noguchi +++ on 3/7/12.	Measles; repeated tonsillitis; joint pains recently.	Pale, nutrition poor; glands +, tonsils +; nose flat, teeth bad and irregular; mitral murmurs, aortic murmurs. ?	Wassermann + 2/13/12	Pirquet +++
22	10	F	Endocarditis, mitral, aortic? 11/22/10	Mother has goiter; two children died at birth. Mother's blood shows Noguchi ++.	Backward; measles and pertussis at 2 years; mumps at 5 yrs. Tonsillitis at 4 and 7 yrs. Scarlet fever 5 mos. ago, followed by polyartic. rheumatism. Blood and albumin in urine 2 mos. ago.	Nutrition poor; pale; tonsils +; teeth notched; mitral murmurs; aortic murmurs; acute nephritis.	Noguchi + 12/15/10	Died 4/9/11

23	9	M	Endocarditis	Four older children healthy; then 2 miscarriages just before birth of patient. Not preg. since patient.	Development normal; chorea 3 mos. ago; edema for 3 weeks.	Nutrition good; tonsils ++; teeth irregular, notched; mitral murmur; glands +; liver +; no spleen.	Noguchi + (weak)	.....
19	1½	M	Congenital heart disease 11/8/10	Paternal G. F. died of heart trouble; mother had one miscarriage at 7 mos.; 1 other child 2 years old healthy. Mother's blood gives positive Noguchi 12/28/10.	Always delicate.	Developm't and nutrition poor; bronchopneumonia; organic heart murmur; spleen +; liver ++.	Noguchi + 12/1/10	Recovery from pneumonia. Died July, 1911, at home.
28	4	M	Tonsils and adenoids	First 4 pregnancies miscarried at 8 mos.; then 5 living children.	Measles, date ? Varicella, date ? Repeated sore throat; adenoid symptoms.	Developm't poor; pale; tonsils +; nose flat; rachitic signs; albuminuria.	Noguchi + 3/5/12	.....
25	¼	F	Rhinitis—"snuffles" 1/16/10	Another child dead at 5 weeks of a bad "cold."	Normal at birth; "snuffles" for 2 weeks.	Nutrition fair; glands +; bronchitis, nasal discharge; no spirochetes found; spleen +.	Sp. Fl. Noguchi + 4/29/10	Left improved 7/17/10
32	11	F	Fracture of ulna 11/30/10	Mother died insane 5 years ago.	?	Pale; "saddle" nose; teeth irregular, notched; glands +; old scars on both shins. Fracture of L. ulna; *x*-ray shows multiple periostitis in both upper limbs.	Noguchi + 11/30/10	Discharged 1/27/11 Improved on Hg.

TABLE 4.—CONTINUED

GROUP III

Case No.	Age, Years	Sex	Admission Diagnosis	Family History	Previous History	Examination	Reaction	Remarks
5	7	M	Tb. Hip	Negative	Measles 1 yr. ago; pertussis; date ? Fall 3 wks. ago; R. hip tender since; lame.	Nutrition good; glands +; teeth irreg. and notched; R. hip tender.	Noguchi +	Pirquet negative
8	4	M	Tb. Spine 5/5/11	?	Measles 1 yr. ago and since, pain in back and can not walk.	Pale, nutrition poor. Chest: enlarged bronchial glands ? Abdomen: Tb? nodules; spleen +; liver +; choked disks (1/20/12, 2/21/12); T. 97-102 F.	Wassermann + 2/24/12	Has had tuberculin regularly since admission to date.
16	11	F	Poliomyeloencephalitis	Negative	Pneumonia; date ? Typhoid date ? Unable to walk for 2 yrs.	Teeth notched and decayed; tonsils +; spastic lower limbs.	Noguchi + 2/9/11	.....
15	10	F	Lesion of spinal cord 9/30/10	Negative	Weak at birth; measles at 7 years; varicella at 9 years; fall 1 yr. ago; since spinal symptoms.	Nutrition poor; paresis R. limbs; teeth notched; glands +; patellar ++; tonsils and adenoids removed; no spirochetes found.	Noguchi + 10/5/10	.....
34	1½	F	Anemia	Negative. Father had 2 negative Wassermanns.	Normal development. For 3 weeks daily rise of temperature; cause ?	Pale; nose flat; tonsils +; dactylitis.	Noguchi + 1/7/11 Wassermann — 1/17/11	Calomel. Tests by different men.
29	2	M	Lobar pneumonia	Negative.	Pneumonia at 1 year.	Nutrition poor; pale; nose flat; vacant stare and "grin"; tonsils+.	Wassermann + 2/19/12	Pirquet negative 2/19/12

3	3	M	Tb. Meningitis 4/4/12	Father had "soft chancre" 7 years before; mother had one miscar.; younger brother died one year ago of "heart trouble"; always delicate.	Gen. development normal; present illness began 7 weeks ago.	Typical meningeal signs; Sp. Fl. clear; lymphocytes; Tb. bacilli? Pirquet negat. Double otitis media.	Sp. Fl. Noguchi +++	Died 4/8/12. Autopsy) showed tb. meningitis, bacilli in exudate at base of brain; no syphilitic changes.
18	½	M	Congenital heart disease 1/4/11	Mother had miscarriage 5 years ago; 3 other child'n healthy; mother died 1 week ago of pneumonia and endocarditis.	Full term, instruments, condition good. Pertussis 3 mos. ago followed by pneumonia. Double otitis, 1 mo.	Nutrition poor; organic heart-signs; ears discharging; weight 10 lbs., 2 oz.	Noguchi + 2/9/11	Left 7/3/11. Mercury from 2/28/11 to 4/6/11
	1¼		10/27/11	.....	.....	Reentered in collapse.	.....	Blood and Sp. Fl. from autopsy negative, by both Wassermann and Noguchi. No syphilitic changes in tissues
24	7	F	Endopericarditis 7/21/11	Mother had 2 miscarriages; poor health since last baby, five years ago.	Measles at 11 mos.; scarlet fever at 4 yrs. Sore throat frequently; for 3 weeks abdominal pain.	Nutrition poor; pale; tonsils +; pericarditis; mitral murmur.	Noguchi + 8/6/11	.....
14	8	M	Epilepsy 3/18/11	Epilepsy in maternal G. M. Mother had petit mal? 3 other children well.	Labor instrumental; mentally slow; measles and scarlet fever 4 yrs. ago; varicella 2 mos. ago; pneumonia 3 mos. ago; "spells" for 2 years.	Head asymmetrical; otitis; pigeon-breast.	Noguchi + 3/9/11	.....
2	12	M	General debility Tb.? 11/14/10	Mother had 3 or 4 miscarriages; 7 other children well.	Developm't backward; dull mentally; pneumonia 4 years ago; scarlet fever 2 years ago; measles 2 years ago.	Poor development; glands +.	Noguchi + 11/26/10	Pirquet + 11/26/10

TABLE 4.—CONTINUED

GROUP V

Case No.	Years Age,	Sex	Admission Diagnosis	Family History	Previous History	Examination	Reaction	Remarks
1	3	M	Miliary Tuberculosis?	Uncle died of phthisis.	Always delicate; typhoid symptoms 3 weeks.	Emaciation; glands+; spleen +; T. 98-104 F.; blood culture neg. Widal negative.	Noguchi +	Pirquet negative left in 1 wk.; unimproved.
7	5	F	Tb. Spine 7/15/10	Negative	Pertussis at 1 year; present trouble began 1½ years ago.	Spinal deformity; glds. +; consolidation R. lung, post. on 1/6/11.	Noguchi + 2/1/11	.....
6	4	F	Tb. Knee	Negative	Development normal; knee symptoms 3 mos.	Pale, nutrition fair; tonsils +.	Wassermann +	Pirquet ++
20	8	M	Endo-pericarditis 3/15/11	Father died of phthisis, 2 years ago.	Weak since 5 yrs. old; measles and diphtheria; rheumatism 1 yr. ago; for 1 mo. cough, pain in chest, weakness, dyspnea.	Pale, nutrition fair; tonsils +, glands +. Endopericarditis.	Noguchi Doubtful—3/29/11 Weakly+4/6/11 Positive 5/11/11	.....
12	4	M	Amaurotic family idiocy 6/24/10	Negative	Always delicate; at 1 week vomiting and convulsions.	Emaciation; eyes show characteristic changes; glands +.	Noguchi — 6/26/10 Noguchi + 1/22/11	Death 9/8/11
10	3	M	Little's disease	?	Always delicate, measles, date ? meningeal symptoms for 2 wks.	Nutrition poor; rigidities; glands +; rickets signs.	Noguchi — 9/5/10 Noguchi + 1/19/11	Pneumonia 1/13/11. Antitoxin.

31	1/6	M	Enterocolitis, Convulsions	Negative.	Well at birth; "cold" for 10 days; convulsions for 24 hours.	Emaciation, pallor; moribund. Sp. Fl. neg. for bacteria; Sp. Fl. pos. for Noguchi.	Blood post-mortem gave positive Noguchi.	Autopsy 10 hours after death; no signs of syphilis.
38	1⅓	M	Rachitis, gastro-enteritis 6/29/10	Negative.	Negative.	Developm't and nutrition poor; rachitic signs; spleen +.	Noguchi ++ 11/28/10	Pirquet negative. Died 2/11/11. Autopsy showed no gross nor microscopic signs of syphilis.
33	7	M	Osteomyelitis 3/27/10 Readmitted 12/7/10	Negative.	Measles at 1½ years; scarlet fever at 3½ years; for 7 mos. pain in legs, fever, sweating.	Nutrition fair; both tibiæ have discharging sinuses. As above.	Noguchi + 12/20/10	Discharged 9/10/10 improved Given Hg. and KI. Improved.
39	5	F	Still's disease	Negative.	Measles 3 years ago; pertussis 2 years ago; for 1 year pain in limbs and joints; unable to walk.	Nutrition poor; rachitic changes; swelling and stiffness of joints.	Noguchi + 10/24/10 1/9/11 Noguchi — 1/19/11	Hg. and KI. from Oct. to March, 1911.

reaction obtained. But against this theory is the fact that specimens of blood from other patients at the hospital, obtained at the same time and handled in the same manner, gave in some instances negative reactions, in other positive reactions. Similarly with the various substances used for antigens, amboceptors, etc.; the same materials used in our cases were used at the same time on patients from another hospital and found to be working well, giving positive reactions on known syphilitics, mostly adults, yet negative results on still others undoubtedly not syphilitic. I have taken pains to "check up" with Dr. Nicoll these points by review of the original records on the given dates of each of the cases in Group V, and it is evident that the error, if error there be, is not in the quality of the different substances used. I cannot be so sure of the absence of error under the first possibility, i. e., some change in the blood used; particularly might this be true with regard to Case 31, when the blood was obtained at autopsy ten hours after death; for Candler and Mann have shown that post-mortem decomposition may alter the reaction whether of the blood or spinal fluid, an ante-mortem positive reaction being converted into a negative, and vice versa.

Taken as a whole, then, Group V may be summarized briefly as follows: There is no ground, except a positive serum reaction, for regarding four of the group, Numbers 1, 12, 20 and 31, as cases of syphilis; there is some ground for regarding the remaining cases as syphilitic, and in them this disease cannot with certainty be excluded. Our third question, then, Does a positive serum reaction, without suggestive physical signs, mean syphilis? must, in the present state of our knowledge, be answered in the negative. Investigations of the future, however, may broaden our conception of the term "suggestive" signs so that it will include signs now not regarded as "suggestive."

NEGATIVE CASES

The negative cases require but little further comment. The diagnoses are given in Table 1. The relative frequency of suggestive family history and suggestive physical examination in the two divisions, positive and negative, has already been noted, there being far fewer such records in the negative than in the positive cases. Among the negative ones were only three cases with such marked physical signs that syphilis could not be excluded. The first of these was a 2-months-old baby, of the Mongolian type of idiocy, with a congenital heart lesion, asymmetrical head, flattened nose and "chicken breast." He was the fifth child, the first

four pregnancies having resulted in miscarriages. The test (Noguchi) was done with his spinal fluid; possibly his blood would have given a positive result.

The second suspicious, yet negative, case was a younger brother of patient, Case 17. He was much below par, with bony changes regarded as rachitic, and with a well-marked syphilitic family history (Table 3, Case 17).

The third case was a 12-year-old girl, of backward development, with marked keratitis and suspicious looking teeth.

RÉSUMÉ

Surveying now as a whole this series of 101 hospital children who have been tested by the Wassermann serum reaction, certain facts strike us.

First, we are impressed with the large number of cases presenting a positive reaction, 38 per cent., over a third, giving such a result. The most of these, as we have seen, we are justified in regarding as syphilis; all, in fact, except the patients in Group V. Deducting the ten cases forming this group, we have twenty-nine (28 per cent.) cases of syphilis among the first hundred children, selected mostly at random, in one of our large American hospitals; that is, nearly one out of every three patients. It has been difficult in the past to obtain an accurate idea of the prevalence of congenital syphilis. That syphilis in general is a lamentably wide-spread disease is well known. Erb, for example, found that out of 10,000 cases of all varieties of disease in his practice, 21 per cent. had syphilis. He believes that 12 per cent. of the adult population of Berlin has syphilis. This means, eventually, a large amount of the congenital form of the disease. Yet it is not generally regarded as being common. Beckel, for example, examined the record of the Babies' Dispensary in Cleveland and found only forty-five cases among 3,500 patients, about 1.33 per cent.; these were all clinical cases and before the days of the serum test.

The observations made in this paper, based on clinical examination and the serum test, would tend to show, however, that there is a large amount of congenital syphilis among hospital patients.

Next we are struck with the great variety of conditions in which we find a positive serum reaction, corresponding with the protean character of syphilis. The greatest number of positive reactions is found, furthermore, in the bony, nervous and circulatory systems, tissues, it will be recalled, particularly apt to be attacked by the syphilitic virus.

The comparatively large number of positive cases without physical signs, the "symptomless" children, is another striking phenomenon, fourteen of the cases (37 per cent.) being so lacking. This again is quite in keeping with the character of congenital syphilis, at least of the late variety, and emphasizes the difficulty of arriving at a diagnosis, and the importance of the serum test in unearthing these obscure cases.

The number of cases reported in this series is, however, small, and it may be that analysis of larger numbers of cases will modify the points which have been discussed, and that the figures obtained in the first hundred cases may be considerably altered by future studies. Enough has been set forth, however, to demonstrate the importance of the serum test in studying our anemic, maldeveloped children and the desirability of applying this test on a large scale to these children, in order, first, to determine to what extent syphilis prevails among them, and, secondly, to institute proper treatment.

The subject is, to my mind, an important one, a broad one; important not only to the victims of the disease itself, but also to the community at large and for the future welfare of the race. If congenital syphilis is nearly as prevalent among certain classes of the community as the studies in this paper would seem to indicate, it is a matter of grave concern to all, especially to us as pediatricians, on whom must devolve the responsibility of determining the extent of the evil and its proper management. We have had put into our hands recently, in the Wassermann serum test, a method of investigation which, together with careful, painstaking clinical observations on a large scale, will give us accurate information, as never before, concerning a malady notoriously fatal in extreme infancy, lamentably blighting in later childhood. But the use of this new weapon must be wide-spread, must be carried out in large numbers of patients before we can answer finally the questions propounded in this paper and the various points suggested by those questions.

This study is therefore offered, not by any means as a final solution of the questions, but rather as a preliminary report, and with the hope that others will also take up and carry on the work.

I am indebted to my fellow members of the Hospital staff for permission to study the children in their wards. I am also greatly indebted to Drs. E. R. LeCount and J. H. Hewitt for the reports on the autopsies.

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DISCUSSION

DR. NICOLL said that personally he could not accept the conclusions drawn by Dr. Churchill, although he did not wish to pose as an expert on the blood diagnosis of syphilis. From what they already knew regarding the reactions of Wassermann and Noguchi those who were constantly in touch with laboratory work did not accept the Noguchi reaction as affording a positive diagnosis of syphilis, acquired or congenital. Dr. Churchill had reported 28 cases on whom the Wassermann reaction was tried, and 62 on whom the Noguchi was used, but he did not state on how many both reactions were tried. He used the term Wassermann as a generic one. In the research laboratory of the Department of Health they did both tests on every case and never reported a case as being one of syphilis on the Noguchi test alone. It was regarded as too delicate. Dr. Churchill had also spoken of the cases of scarlet fever giving a positive Wassermann reaction, but there was no good evidence that scarlet fever *per se* would give a reaction similar to what was obtained in cases of syphilis. In looking over the list of Dr. Churchill's cases he said he could not regard them as fair examples of the general run of hospital cases. There were too many chronic cases and too many examples of pathologic conditions which might well be attributed to syphilis. In regard to tuberculosis, especially of bone, there seemed to be some reason for believing that a positive Noguchi reaction might be obtained without the presence of syphilis

DR. HOLT said that most of the cases on the list were examples of chronic disease. He did not think that routine cases from an acute service would show so large a proportion of positive results.

DR. FREEMAN said that many children were seen at the New York Foundling Hospital on whom a clinical diagnosis of syphilis was made. They had snuffles, the shiny red appearance of the soles and palms, desquamation of the skin, sores about the anus, and that they did badly unless put on inunctions. A very competent pathologist of this institution had recently been examining cases and had obtained negative results from microscopic examinations; nevertheless the speaker believed them to be cases of true syphilis.

DR. CHURCHILL, closing the discussion, said that he did not feel competent personally to pass on the comparative value of the Noguchi and Wassermann reactions, but from a study of the literature embracing at least 2,000 cases it seemed

that the Noguchi test was as reliable as the Wassermann. With regard to the reaction occurring in scarlet fever, it did occur; though not commonly. With regard to the so-called selected cases, he said he did not know how large a hospital service Dr. Nicoll had, but he thought his list was quite characteristic of the general run of cases entering the hospital. The cases were not picked out, but were taken as they came, with but few exceptions. With regard to the autopsy findings, one could not draw any conclusions from three instances.

THE EMPLOYMENT OF SALVARSAN IN INFANTS AND YOUNG CHILDREN *

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If we consider only the moderate grades of congenital syphilis, the treatment of the disease by the older methods with the various preparations of mercury and iodid of potash has been quite satisfactory. When, however, we consider the severer types, particularly those showing a tendency to hemorrhage during the early days of life, and when, moreover, we contemplate the possibility of the appearance during the latter part of the first decade of the tardy manifestations of the disease, a feeling of dissatisfaction must come to us. On account of the high mortality of the serious cases, on account of the possibility of late manifestations of the disease in the eye, ear, bones or nervous system, there has long been needed, even in the management of lues in infants, some other more powerful and more certain remedy.

Moreover, since the introduction of the Wassermann reaction for the detection of the disease and also for determining that the disease has been checked, if not eradicated, there has been a still further incentive toward the use of other than the mercurial treatment. It was Ehrlich's hope that in "606," or salvarsan, he had obtained the great sterilizing agent which would by one administration, if in sufficient dosage, entirely destroy the spirochætæ and so rid the system of the disease and of its consequences.

The use of salvarsan in adults has been so general during the past two years that very definite conclusions have been reached in regard to technique and dosage. With regard to the use of salvarsan in infants, however, there is not as yet the same certainty in this respect.

The salvarsan may be administered to the infant indirectly by injection of the pregnant or of the nursing mother, or it may be given directly to the infant.

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*From the Children's Wards of Bellevue Hospital, First Medical Division.

According to the conclusions of De Buys[1] the results on the infant of injecting the pregnant woman with salvarsan have been generally unfavorable. He quotes Gluck as having injected a woman seven months pregnant with resulting death of the fetus on the following day.

Good results from injecting the nursing mother have been reported by Taege,[2] Duhot,[3] Malinowski,[4] Dobrovits,[5] Sequeira,[6] Marschalko,[7] and others. Negative results from the indirect method are reported by Peiser,[8] Rosenthal,[9] Ritter.[10] Oppenheim,[11] and Spiethoff[12] report negative results by the injection of the mother, with later good results after direct injection of the infants.

The best and most rapid results are obtained by the direct injection of salvarsan into the infant. The routes for injection have been the subcutaneous, the intramuscular and the intravenous. The subcutaneous injections produced bad sloughs or cellulitis and so were soon abandoned. The intramuscular (usually intragluteal) injection of a paraffin oil emulsion of salvarsan in dosage of 0.015 gram per kilogram is favored by Hochsinger[13] and others, while von Bokay[14] prefers Wechselmann's neutral suspension in dosage of 0.008 to 0.01 per kilogram. Von Bokay used this method in twenty-six cases, giving second injections in ten instances, and seems enthusiastic over the direct method, though the occurrence of three relapses leads him to the conclusion that the ideal procedure with salvarsan has not yet been determined.

Savariaud[15] reports a good result by direct treatment of a girl of 4 years suffering from bone lesions after mercurial treatment had been unavailing.

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1. De Buys: Arch. Pediat., 1911, p. 920.
2. Taege: München. med. Wchnschr., 1910, No. 33.
3. Duhot: München. med. Wchnschr., 1910, No. 35.
4. Malinowski: Monats. für prakt. Dermat., 1911, Part III, p. 101.
5. Dobrovits: Wien. med. Wchnschr., 1910, No. 38.
6. Sequeira: British Jour. Child. Dis., 1911, VIII, 49.
7. Marschalko: Deutsch. med. Wchnschr., 1911, No. 5.
8. Peiser: Berlin. klin. Wchnschr, 1911, No. 1.
9. Rosenthal: Berlin. klin. Wchnschr., 1910, No. 47.
10. Ritter: Berlin. klin. Wchnschr., 1910, No. 51.
11. Oppenheim: Med. Klin., 1911, No. 8.
12. Spiethoff: München. med. Wchnschr., 1910, No. 35.
13. Hochsinger: Wien. med. Wchnschr., 1911, p. 122.
14. Bokay: Wien. klin. Wchnschr., 1911, XXIV, No. 17.
15. Savariaud: Bull. Soc. de pediat. de Paris, 1911, p. 93.

Among others who reported good results from the direct method are Escherich,[16] six cases; Lesser,[17] nine cases, and Miekley,[18] five cases.

Toxic polyneuritis from the intragluteal injection of 0.3 gram in an 18-months-old girl has been reported by Fischer,[19] and parenchymatous nephritis along with necrosis of the subcutaneous fat, muscles, blood-vessels and nerves has been reported by Merkel[20] as the result of the intragluteal injection of salvarsan in a 2½-months-old infant.

Since June 30, 1911, there have been treated on my service in the children's wards at Bellevue Hospital twenty-five cases of hereditary syphilis of the congenital type. Of these, ten received salvarsan either with or without mercurial treatment, while fifteen were treated by the use of mercurials alone. It should be said in explanation of the large number that did not receive salvarsan treatment, that some of these patients were in a moribund condition and died within two or three days after entering the hospital, even before a Wassermann reaction could be obtained; others were such mild cases that it seemed wise to use only mercury; while for still others there was objection on the part of the parents to the admistration of the new remedy intravenously.

The ages of the fifteen patients in whom only mercurial treatment was used ranged from three weeks to one year—the most of the patients being about 3 months old. The ages of the ten salvarsan cases ranged from 2 months to 5½ years.

The two sets of cases were treated in the wards side by side without selection, save that the moribund cases were not given salvarsan.

The symptoms of the infants and younger children were quite similar in the two groups of cases, with the exception that the one patient 5½ years old receiving salvarsan had severe bone lesions.

The mercurial treatment consisted usually in the administration of gray powder ¼ to ½ grain two or three times daily, together with inunctions of 25 per cent. blue ointment every second day. In some cases the salicylate of mercury was injected intramuscularly in doses of 1/10 of a grain every second day.

16. Escherich: Wien. med. Wchnschr., 1910, No. 46.
17. Lesser: München. med. Wchnschr., 1911, No. 1.
18. Miekley: Deutsch. med. Wchnschr., 1910, No. 41.
19. Fischer: Jour. Am. Med. Assn., 1911, LVI, 455.
20. Merkel: München. med. Wchnschr., 1911, No. 15.

The technique of the salvarsan administration was as follows:

Only freshly distilled water, heated up to 120 F., was used in making up the solution.

The contents of the ampulla of salvarsan, containing 0.6 gram of the drug, are poured into 100 c.c. of the hot water and then shaken thoroughly until dissolved. Four per cent. NaOH solution is then added cautiously until the fluid is clear. It usually takes about 0.7 c.c. of the 4 per cent. NaOH solution to each 0.1 gram of salvarsan, or about 4 to 4.5 c.c. of the NaOH solution to alkalinize the 0.6 gram salvarsan in the ordinary ampulla. Then more hot distilled H_2O up to 300 c.c. Each 50 c.c. of this solution represents 0.1 gram, or each 5 c.c. represents 0.1 gram of salvarsan, which is convenient for dosage. The cloudiness often found in the salvarsan solution is filtered out through sterile gauze. Now the solution is ready for injection. It is most convenient to make use of an apparatus devised by Dr. Albert M. Meads, of Bellevue Hospital, New York, who has, since December, 1911, given forty-three injections with it. This consists of two tall 300 c.c. vessels, one for the salvarsan solution and the other for salt solution, connected by tubes to a Y, from which passes the long tube carrying the needle for injection. Both vessels are connected at the top with a tube leading to a pressure bulb which can be used to hurry the liquids out of the vessels. When the patient's vein is ready, some 0.9 per cent. NaCl solution is run through the long tube. Next, plunge in the needle and run in a little NaCl solution, then turn stopcock and run in the desired amount of salvarsan solution. Then run in more NaCl solution to force the salvarsan further into the general circulation, and out of the vein.

There is seldom any rise of temperature afterward, in most cases none at all. At times a rise of temperature the same day may be due to the mere excitement of the operation itself.

Because of the disastrous or unsatisfactory experiences of others, none of the salvarsan was given intramuscularly nor subcutaneously. It was always given intravenously and nearly always after having cut down and exposed a vein at the bend of the elbow. To plunge the needle through the skin and subcutaneous fat and into the vein is not easy in infants, since the vein slips away or else is pierced clear through. Recently it has been proposed to use the vein of the scalp, and no doubt this will simplify the administration in many cases.

The ages, the weight of the patients and the dosage employed were as follows:

Case	Age	Weight	Dose gm.
1	2 mos.	9 lbs., or about 4½ kg	0.05
2	9 mos.	7-8 lbs., or about 3¾ kg	0.05
3	3 yrs.	25 lbs., or about 12 kg	0.10
4	2 yrs.	23 lbs., or about 11½ kg	0.10
5	2 yrs.	23 lbs.. or about 11½ kg	0.08
6	3 mos.	9 lbs.. or about 4½ kg	0.05
		on Oct. 12, and second dose, Dec. 18	0.05
7	5½ yrs.	27 lbs., or about 13 kg	0.10
		on Oct. 22, and second dose, Jan. 7, 1912,	0.10
8	17 mos.	17 lbs., or about 8 kg	0.10
9	2 mos.	8 lbs., or about 4 kg	0.10
10	11 mos.	9 lbs., or about 4½ kg	0.10

These last two doses were nearly double the proportions used before.

Reaction to the Intravenous Injection.—As regards local or general reaction from the intravenous injection, there was never any necrosis or inflammation at the site of venipuncture, and the febrile reaction spoken of by many authors was seen only three times, even then being very mild, a rise on same day to 103 F. in one case and up to 101 or 102 F. in two cases on the second or third day after injection. The absence of febrile reaction is thought to be due to the use of freshly distilled water for making up the solution.

In one case in which there had been an irregular fever up to 102½ F. before the injection, the temperature gradually came down to normal after injection, coincidently with the disappearance of the snuffles and the fading of the maculopapular eruption.

The results of the fifteen cases treated by mercurials alone were as follows: Three improved, two unimproved and ten died. The ten cases treated by salvarsan showed a mortality of only two; all the other cases were decidedly improved and several showed marked gain in weight and improvement in general condition in addition to the disappearance of their specific symptoms.

One child 2 years old gained 5 pounds in weight in two and one-half months, though the Wassermann remained positive until time of discharge from the hospital.

The 5½-year-old child gained in weight from 27 to 36 pounds during her six months' stay in the hospital, having had two salvarsan injections and later protoiodid of mercury pushed to the limit of tolerance.

Another child, 17 months old, gained nearly a pound in her short sojourn of nine days in the hospital.

The detailed record of the 5½-year-old child seems worth reporting, since it showed a relapse of symptoms while under observation and most marked improvement by the employment of both salvarsan and mercurial treatment.

Fig. 1.—Photograph showing saddle nose and marked swelling of radius and ulna of left forearm.

Jeannette K., 5½ years old. Admitted Oct. 12, 1911. Discharged improved April 9, 1912.

Family history of two still-births and of two other children dead of convulsions.

Previous personal history not obtainable further than that the child had suffered from painful swollen wrists and joints for some months. Both wrists were swollen, together with the bones just above the wrist, and on the right side there was a tender fluctuating swelling.

Fig. 2.—Radiogram of left forearm, showing the thickening and destruction of lower ends of radius and ulna.

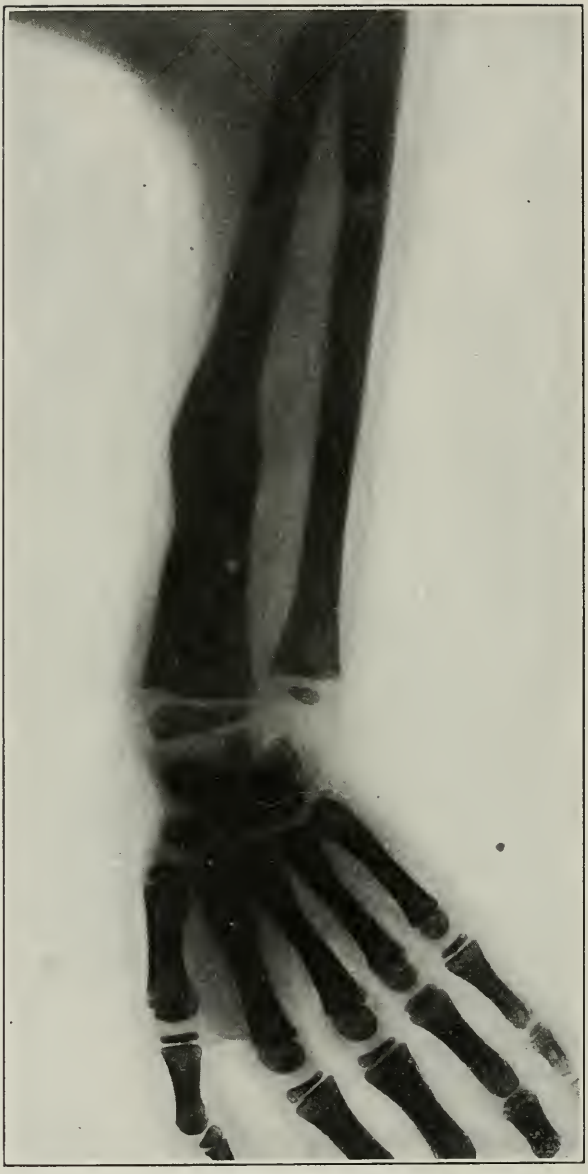

Fig. 3.—Radiogram of right forearm, showing thickening of shaft of radius.

Fig. 4.—Radiogram of right forearm, taken four months after Fig. 3, and showing improvement in shaft of radius.

Saddle nose, enlarged spleen, liver and lymph-nodes, together with some swelling of the bones of legs completed the picture of late hereditary lues.

The photograph taken November 1 shows fairly well the surface appearance of the forearms. (Fig. 1.)

X-ray pictures taken two days after admission showed characteristic bone changes—subperiosteal infiltration with osteoporosis especially marked at the lower ends of the greatly thickened ulna and radius. (Figs. 2 and 3.)

On October 15, three days after admission, the Wassermann reaction was found to be positive, though only weakly so.

On October 22, 0.10 gram salvarsan was given intravenously, and that same night there was a temperature reaction up to 103 F. This lasted only a few hours, and on the following day the temperature was normal. The tenderness and swelling in the forearms improved rapidly, but on December 5 the *x*-ray showed that there had been only slight improvement in the condition of the bones.

On December 11 the Wassermann test was still positive.

On January 5, 1912, on account of a very definite relapse of the forearms to a condition almost as bad as on admission to the hospital, a second injection of salvarsan was given—the same amount as at first, 0.10 gram, was injected intravenously.

This time there was absolutely *no* temperature reaction. Now in addition to the salvarsan there was given for a few days before the second salvarsan injection protoiodid of mercury, 1/10 grain *t.i.d.*, later increased to 1/5 grain *t.i.d.* This was continued until mild symptoms of salivation showed themselves, about March 23.

The improvement after the second injection, and coincident with the administration of protoiodid was rapid and continuous, so that the bones of forearms and legs became normal to ordinary physical examination. The Wassermann reaction became negative and was still negative on May 20. Unfortunately, the child was removed from the hospital unexpectedly, so that I am unable to exhibit *x*-ray pictures showing the condition on discharge. The improvement in the condition of the right forearm is shown in Figure 4.

The case would seem to indicate, however, (1) that the initial dose was too small, and (2) that supplementary treatment by mercury and iodids is of great advantage.

The *Wassermann reaction* before the salvarsan injection cases was negative in two cases, negative in another on October 4, and positive on October 20; positive in three besides the alternating case just mentioned and not obtained or doubtful in four. The clinical features of the disease were perfectly typical in the cases that had a negative Wassermann.

After the injection of salvarsan in the dosage mentioned, the Wassermann was found to be still positive in two out of the three cases in which the reaction was tested. In both these cases the clinical symptoms of the disease had entirely disappeared.

In only one case, that of the child 5½ years old, did the Wassermann reaction become negative, and from the reports of other observers there is no assurance that this disappearance is permanent.

Before closing I wish to express my thanks to my resident physician, Dr. Miner C. Hill, who carried out ably and skilfully the details of treatment; to Dr. I. Hirsch for the excellent radiograms, and to Dr. Gus R. Manning, who assisted me in looking up the literature.

CONCLUSIONS

1. While the indirect method of giving salvarsan to the nursing mother is valuable and should be used when the mother is available, the surest method consists in giving the salvarsan to the infant. Both indirect and direct administration should be employed whenever possible.

2. The intravenous route of administration is the best. Usually it will be found easiest to expose the vein before attempting to insert the needle.

3. The dosage should be not less than 0.01 gram per kilogram of body weight.

4. Repeated injections and supplemental treatment by mercurials may be necessary.

5. The Wassermann reaction should be followed for a year.

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DISCUSSION

Dr. Holt reported on thirty-seven injections of salvarsan that had been made in twenty-four patients at the Babies' Hospital. Seventeen of the patients were under 1 year old and four of them were under 1 month. On account of extensive sloughing which had been seen after their use, intramuscular injections had been given up and all of these patients had been treated by intravenous injections. The introduction of the needle into the vein of an infant had been found extremely difficult and unsatisfactory and it had been replaced by a small glass cannula similar to that employed for transfusion.

In these small patients a dissection of the vein had been found necessary and for this general anesthesia was desirable. Local anesthesia was at first tried but was not satisfactory. No reactions worth the name were observed. Only twice did the temperature rise above 101 F. and then only for a few hours. A slight infiltration occurred about the vein in one instance, but this passed away after two or three days. In no other case was there any local or general reaction. The wound in every instance healed by first intention. Other treatment was adopted in all but three cases, it having been the experience at the hospital that the best results were obtained by this combination treatment. In some instances striking benefit followed the injection of salvarsan when no other treatment was employed. Thus one child, 13 months old, was admitted with a very large liver and spleen; marked secondary anemia; large epitrochlear glands; positive Wassermann; the spirochetes were obtained in the epitrochlear glands. A single injection was given resulting in rapid improvement in all symptoms and a gain of 19 ounces in weight

in two weeks. The father had definite signs of syphilis in this case. Another infant, aged 3 months, had pseudoparalysis of both upper extremities almost complete; movement caused pain, somewhat suggesting scurvy; liver and spleen enlarged; general condition good. Two weeks after injection the paralysis disappeared. While experience was not broad enough to determine accurately the place of salvarsan in the treatment of hereditary syphilis, it was found of the greatest advantage especially in cases where urgent symptoms existed; but the best results were obtained where it was combined with other treatment. The dose of salvarsan employed had been grams 1/20 for infants under six months and 1/10 for those under one year; second injections were given in seven patients, and a third injection in three patients.

Dr. Butterworth said that only those who had tried to enter the veins of the upper extremities realized the difficulties encountered and he advised the use of the vein over the internal malleolus which gave very satisfactory results.

He believed, judging from his experience with quite a large number of cases, that the repeated injection of small doses of salvarsan was better than the giving of the larger doses. The simplicity of the apparatus presented commended itself to him.

Dr. Abt asked how old the children were.

Dr. LaFétra replied that the ages ranged from 6 weeks to 2 years, one child being 5½ years old. The reason the apparatus shown was commended was because with it several injections could be given successfully without refilling. The apparatus shown by Dr. Holt could contain only what was sufficient for one injection, or one dose. The use of the glass tube was undoubtedly a great advantage because the fluid could flow through with greater facility and no pressure was necessary. As he had stated in his conclusions, it was better to use salvarsan in conjunction with the use of mercury.

FURTHER REPORT ON THE CASE OF DIABETES MELLITUS IN AN INFANT PRESENTED AT THE LAST ANNUAL MEETING

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I wish to make a further brief report of the case presented to you a year ago, having received under date of May 20, a letter from the physician in charge of the case. The baby is now 24 months of age and is reported to be better in many respects, although he eliminates considerable sugar, acetone and diacetic acid. He has been weaned and is now on a general non-carbohydrate diet, with the exception of oatmeal, which he takes at times and in considerable quantities. He is not so troublesome as when at the breast. He now has all his teeth, but during the time when the teeth were coming through the gums he always seemed sicker than usual, and several times has seemed on the point of coma. The physician would then push the bicorbonate of soda solution, when the condition would improve at once. He has had a great deal of papular and pustular involvement of the skin for which a streptococcus vaccine was used with seeming improvement in his general condition. He is said to digest everything he eats and on the whole is doing very well. The last specimen examined about May 10, had a specific gravity of 1,030: acetone, and diacetic acid present. This report is of interest mainly because the child is still living and doing very well, while as a rule, they do not survive this length of time.

Note (by Dr. Eaton, Aug. 15, 1912).—A few days ago I received a letter from Dr. Stahlman of Vandergrift, Pa., telling me of the death of the baby. Dr. Stahlman writes that the baby died July 24, having developed diabetic coma the day before. This last attack of coma was the third it had had, but was much more severe than the others. He also noted that a few weeks before the end, the baby had a discharge of pus from both ears, and that the glands low and behind the ears seemed to be involved.

DISCUSSION

Dr. Kerley said that the two cases that he had previously reported to the Society were still alive and doing well. The older brother was at Columbia University and was an athlete of no small promise. Both boys had shown diacetic acid in small amounts in the urine. Both were big husky fellows.

AN EARLY CASE OF CHONDRODYSTROPHY WITH RADIOGRAM AND NECROPSY

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History.—The subject of this report, R. B., was admitted to the Infants' Ward of Bellevue Hospital, Nov. 1, 1911, five hours after birth. She was said to have been born at full term, and was delivered without difficulty by a midwife. As to the family history, there had been three other children, all of whom were dead, one at ten months and the other two, which were twins, at 2 months. No miscarriages nor stillbirths. There is no history of any similar deformities in the family and there are no dwarfs in the family connection; also no history of tuberculosis, syphilis nor any other constitutional disease.

Physical Examination.—Well nourished infant, the general appearance of the trunk resembling a seal. The skin is very cyanotic and the most striking feature about the face is the marked exophthalmos. The nose is short and saddle-shaped, with a deep depression at its root. The soft palate is fissured up to the posterior margin of the hard palate. The tongue is very large, filling up the entire posterior pharynx.

The heart sounds are normal; no murmur.

The liver is palpable at edge of costal margin; the spleen is not felt.

All the bones of the extremities are exceedingly short and their diameter is comparatively large; the flat surface of the long bones is wider than normal and the bones themselves are bowed, the normal curves being greatly exaggeration. The bowing is most marked at the epiphyseal ends of the bones.

The humerus is very short and the finger tips reach only to the crest of the ilium.

The left tibia is so short and so bent on itself that one's forefinger, if laid on the internal surface of the bone, is found to be simultaneously in contact with the upper tuberosity, with the shaft and with the internal malleolus.

Measurements: Head, circumference, 41.5 cm.; bitemporal diameter, 9 cm.; biparietal diameter, 11.3 cm., occipito-frontal, 12.7 cm.; occipito-bregmatic, 10.7 cm.; occipito-mental, 13.5 cm.; anterior fontanel, 6.3 cm.; posterior fontanel, 1.5 cm. long; bisacromial diameter, 12.7 cm.

Length: Crown of head to umbilicus, 25.2 cm.; umbilicus to sole of foot, 15.0 cm.; acromion-olecranon (arm-length), 6.3 cm.; diameter, 9.3 cm.; olecranon-wrist (forearm-length) 4.5 cm.; diameter, 8.3 cm.; hand, 5 cm. long; diameter, 7.5 cm.

Lower Extremity: Anterior superior spine to condyle, 7.5 cm.; circumference, 13.0 cm.; condyle to ankle, 7.5 cm.; circumference, 9.5 cm.; foot, 6.3 cm. long; diameter, 7.5 cm.

The thorax at nipple is 26.5 cm. in circumference; expansion is about 2 cm. December 19, the hemoglobin was 65 per cent.; red cells, 5,700,000; white cells, 17,400.

Fig. 1.—Photograph taken at 1 week. It shows the exophthalmos, the pug nose, and the very short arm and forearm. The finger tips reach only to the crest of the ilium, and the fingers are not separated to form the "main en trident."

While in the hospital the baby was fed almost entirely on breast milk; but it gradually lost weight and died without symptoms of any definite disease at the age of 10 weeks. The weight on admission was 5 pounds, 4½ ounces; it had fallen to 4 pounds, 12 ounces before death.

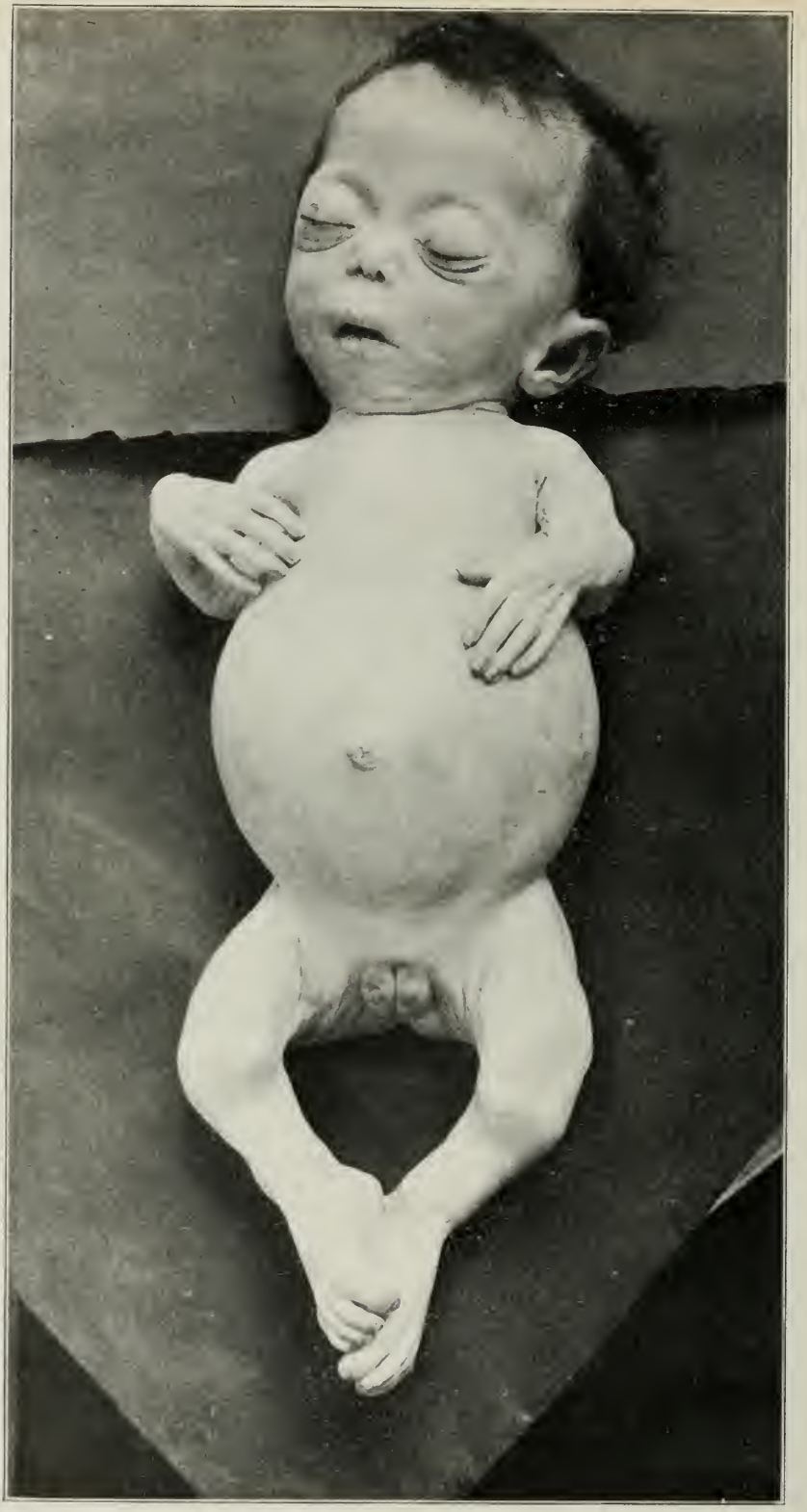

Fig. 2.—Photograph taken after death at 10 weeks. It shows also the marked thickening and bowing of the tibiæ.

Radiographic examination of the whole body was made Nov. 9, 1911, by Dr. I. S. Hirsch, radiographer of Bellevue Hospital, whom I wish to thank for his skilfull work. His report is as follows:

RADIOGRAPHER'S REPORT

"The radiograph shows all the essential bony and joint changes characteristic of achondroplasia. There are no points of ossification for the epiphyses of any of the bones of the upper extremity; but the lower epiphyses of the femora are partially ossified. The diaphyseal portions of the bones are broadened and sharply outlined."

The *x*-ray print shows particularly well the shortening and thickening of the long bones. For comparison there is presented also the *x*-ray print of a normal though premature infant of practically the same length.

PATHOLOGIST'S REPORT

Necropsy.—I wish to thank Dr. Charles Norris, the Pathologist of Bellevue Hospital, for his careful autopsy, for his interest and help in the study of the case, and for permission to make an abstract of the post-mortem record as follows:

Anatomic Diagnosis.—Chondrodystrophia congenitalis; rachitis.[1]

The body is that of a female child, 42 cm. long and weighing 2,270 gm. No description of the skeletal changes will be given because of the excellent *x*-ray photograph of the cadaver.

There is a very marked exophthalmus. Pupils normal. There are no external congenital anomalies. The vulvæ are large and swollen. The anterior fontanel is large, 5 cm. in width by 6 cm. anteroposteriorly. The posterior fontanelle is very small, but open. The sutures are wide. The face is of normal size. The right ear is thickened and red, showing a few superficial ulcerations on the antitragus. The left ear is normal.

There is a marked rosary, the swelling of the costochondral junctions being most marked internally. The ribs are long. There is a longitudinal groove just external to the costochondral junctions, but there is no Harrison's groove. The small intestines are markedly distended with gas. The peritoneal cavity contains blood-stained fluid (possibly due to post-mortem changes and freezing, the body having been frozen). The urachus is persistent, for a distance of about 1 inch. The cord is normal. There is a small umbilical vein. The sigmoid flexure is very long, extending well into the right side. The mucosa of the small and large intestines is everywhere very smooth, there being no solitary follicles or Peyer's patches visible.

Spleen: Weight 10 gm. It is 56 mm. by 25 mm. It is firm, dark red on section. No splenic follicles are visible.

Liver: Weight 90 gm., normal in size, dark red in color; serosa is everywhere normal and glistening; section dark red and smooth, without gross lesions.

Gall Bladder: This viscus is normal.

The mesenteric lymph nodes are everywhere small and somewhat yellowish in color.

1. For correction of this gross anatomical diagnosis, see note in microscopical examination.

Lungs.—The lungs show normal lobulations. The left lower lobe is completely atelectatic, red, firm, smooth on section, with extreme congestion. The posterior borders of all the lobes of the right lung are atelectatic. Otherwise the lungs and bronchi are normal.

Fig. 3.—*X*-ray print of patient when 8 days old. It shows the characteristic shortening and thickening of the long bones.

Heart: There is no fluid in the pericardial cavity. The heart is possibly somewhat enlarged. The apex is formed by the left ventricle. There is a moderate

Rechtslage, the aorta being visible and to the right of the pulmonary arteries. The right heart is somewhat large. There is a small foramen ovale. The ductus botalli is large. There is no stenosis of the isthmus. All the valves of the heart are normal. Musculature of the heart normal. The aorta and the vessels given off from the aorta are normal in distribution and appearance.

Pancreas: Weighs 5 gm.; is small; the lobulations are possibly not well developed. The head of the pancreas is somewhat red (post-mortem changes?).

Adrenals: The left adrenal weighs somewhat less than 2 gm., the right 1.25 gm. The left measures 32x25 mm., the right 15x13 mm. The cortex is very thin and pale. The medulla of both adrenals is hyperemic. There is almost no perirenal fat.

Kidney: The left kidney shows slight fetal lobulation. The pyramids are normal. Weight 13 grams.. The right kidney was not measured but appears to be of the same size and is similar in gross appearance.

The genital organs show no anomalies.

The thyroid gland is very small. The lobes are symmetrical. Both lobes weigh 1 gram. Thymus is small; weight 5½ grams. There appears to be almost no glandular tissue present. The fat of the anterior mediastinum is edematous. The tongue is about normal in size. Both tonsils are extremely small. The pharynx and larynx are normal. There is no hyperplasia of the lymphatic apparatus. The parathyroids were dissected out, seven being found.

Although there was no edema of the skin of the legs or arms, the subcutaneous tissues of the thorax and other portions of the body are everywhere slightly moist or edematous.

Head: Superficial examination of the brain, which was not opened until hardened, reveals no gross lesions. The dura appears everywhere to be slightly thickened. The foramen magnum is very narrow, showing marked irregularity; and the clivus is steep.

The foramen magnum is very peculiar, being distorted and irregular. The basilar portion of the ring is at a level 6 mm. below the occipital, and the shelving occipital portion is obliquely placed, so that the opening for the cord is oblique, its sagittal diameter running from the left anteriorly to the right posteriorly. This diameter measures 6 mm., while the longer obliquely transverse diameter measures 11 mm. The steep clivus is 28 mm. long.

On microscopic examination the thyroid gland shows an advanced grade of interstitial thyroiditis.

There is also an infiltration of small round-cells in the subcutaneous tissue and in the muscles, those from the abdominal wall alone being examined. Similar changes have been described in myxedema.

As to the gross anatomic diagnosis of rachitis, it should be recorded that the sections taken from the costochondral junctions and from the femur show no evidence of rachitis, the lesion being characteristic of chondrodystrophy with an extreme grade of mucous degeneration of the cartilage cells.

The case reported, while exhibiting the characteristic features of chondrodystrophy, must be regarded, in view of the gross and microscopic examination, as one of mixed type. There is no redundancy of skin on the lower extremities, there is no trident hand; there is a congenital anomaly in the cleft palate, and there is evidence of thyroid deficiency which has probably no etiological significance. The general subject of

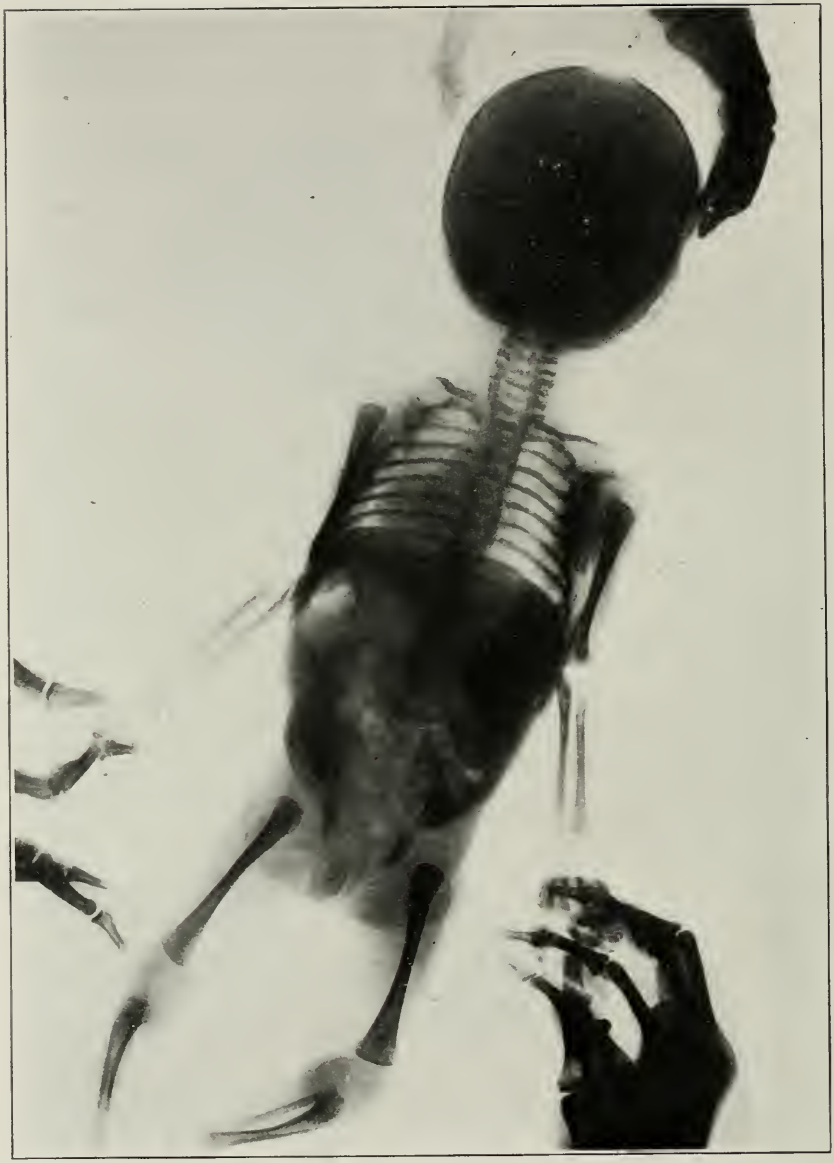

Fig. 4.—X-ray print of healthy premature infant 14 days old, for comparison of long bones. The infant was 44 cm. long, or only 2 cm. longer than the chondrodystrophic infant.

chondrodystrophy has been so thoroughly discussed in recent literature that here no description of the disease will be attempted. For a full consideration of the subject the reader is referred to Kaufmann's monograph on "Chondŷstrophia Fœtalis," and to the admirable volume on "Dwarfism" in the Eugenics Laboratory Memoirs XV, Section XV, a. Here will be found a complete discussion of achondroplasia by Dr. H. Rischbieth, together with a résumé by Amy Barrington of the Bibliography of Dwarfism, and reproductions or descriptions of the dwarfs (mostly chondrodystrophic) depicted by famous painters.

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ON THE MODE OF INFECTION IN EPIDEMIC CEREBRO-SPINAL MENINGITIS

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The *Diplococcus intracellularis* was identified as the specific excitant of epidemic cerebrospinal meningitis by Weichselbaum in 1887. The procedure of lumbar puncture as a means of obtaining cerebrospinal fluid and attaining an etiologic diagnosis in cases of meningitis was introduced by Quincke in 1891.

The studies of meningitis made possible by this means have established beyond question the relationship of the meningococcus to the epidemic type of meningitis which has presented itself in various parts of the world during the last decade. As this relationship has been made clear, the problem of the control of this dreaded disease has focused itself about the life of the specific organism, its distribution in the body of those affected by the disease, its paths of exit from the body, its viability, and the mode by which the infection might be conveyed to others. Most of the points of interest and importance in these relations have been quite thoroughly cleared up.

The meningococcus has been found not only in the cerebrospinal fluid of those suffering from the disease but in the conjunctiva and the eye, in the nose and throat, in the pleura and lungs, in the pus of joints, in the throat, and in the blood. So far as our present knowledge leads us, the organism may be excreted from the body by the purulent discharges from an active conjunctivitis or by the secretions of the nose, throat and bronchi. While the organism has been found in the conjunctival secretions by Koplik,[1] Robinson,[2] and others, and the possibility of contagion from that source must be recognized, active conjunctivitis is not a frequent accompaniment of the disease and infection from that source must be rare.

In like manner, as Jakobitz[3] has shown, the meningococcus may be found in the lungs both in those suffering from cerebrospinal meningitis, with or without definite pulmonary complications, and in rare instances

1. Koplik: Osler's Mod. Med., ii, 499.
2. Robinson: Am. Jour. Med. Sc., 1906, cxxxi, 603.
3. Jakobitz: Ztschr. f. Hyg. u. Infectionskrankh., 1907, lvi, 175.

in pneumonias and bronchial catarrhs occurring independently of meningitis.

The greatest interest and importance, however, attach to the presence of the meningococcus in the nose and throat, because its presence in these passages may not only be a ready means of disseminating the organism outside the body of the patient, but also suggests the possibility of direct infection of the meninges from this source.

Since von Lingelsheim directed attention to the fact that the organism was to be sought not in the nares but in the nasopharynx, the reports of its discovery in cases of meningitis have shown increasing positive results. With the question of the identification of the *Diplococcus intracellularis* we need not here concern ourselves. The work of Councilman, Mallory and Wright,[4] Albrecht and Ghon,[5] and von Bettencourt and Franca[6] has made the differentiation of the meningococcus so certain that reports conforming to the established standards can be accepted as reliable.

From reports of the occasional finding of the specific organism in the nasal or nasopharyngeal secretions, we find more and more positive results recorded. Thus Goodwin and von Scholly[7] obtained positive results from the nasal mucus of twenty-seven out of fifty-two (50 per cent., plus) cases examined during the first two weeks of the disease and Dieudonné[8] four positive findings in six cases (67 per cent), and von Linglesheim[9] under favorable conditions forty-six positive results in forty-nine examinations (93.8 per cent.). It seems probable that the organism is present in the nose or nasopharynx of most of the cases of epidemic meningitis during the early stages of the disease.

But it has also been found in the same site in well persons, especially in those who have been in contact with cases of meningitis and also in many in whom no knowledge of exposure can be obtained. Thus Goodwin and von Scholly found the specific organism in the nasal secretions of 10 per cent. of forty-five "contacts;" Dieudonné obtained five

4. Councilman, Mallory and Wright: Epidemic Cerebrospinal Meningitis, Rep. Mass. St. Bd. Health, Boston, 1898

5. Albrecht and Ghon: Wein. klin. Wchnschr., 1901, xiv, 984.

6. Von Bettencourt and Franca: Ztschr. f. Hyg. u. Infections-krankh., 1904, xlvi, 463.

7. Goodwin and von Scholly: Jour. Infect. Dis., 1906, p. 21.

8. Dieudonné: Centralbl. f. Bakteriol., 1906, xli, Pt. 1, 418.

9. Von Linglesheim: Klin. Jahrb., 1906, xv, 400.

positive results in thirty-nine trials, and Fraser and Comrie[10] ten in sixty-nine trials, of contacts.

In the effort to control the inroads of the disease in the German army, similar investigations have been made on a large scale in regiments exposed to the disease, with most interesting results. Hübener and Kutscher[11] report that in 400 men of one batallion they found eight coccus carriers although there were no cases of meningitis in the regiment itself at the time, and Vagedes[12] in 1,703 men examined under like conditions found ten carriers.

Under ordinary conditions the meningococcus quickly perishes outside the human body. It therefore seems highly probable that the spread of the disease depends on the presence of the specific organism in the nasal passages or respiratory tract of those sick with the disease and also of many persons in good health. The respiratory tract, and especially the nasopharynx, appears to be the usual portal of entry.

These facts being accepted, how does the organism from the nasopharynx or other part of the respiratory tract reach the meninges and there set up its specific inflammation?

The proximity of the nasopharynx to the meninges naturally suggested the possibility of direct infection. Of many contributions to the discussion of this subject, that of Westenhoeffer[13] is based on the study of the most ample material and is of most interest.

As the results of his anatomic observations, Westenhoeffer lays emphasis on the following facts:

1. The meningitis begins at the base of the brain, in the region of the optic chiasm and about the hypophysis cerebri, and from this point spreads in all directions.

2. There is a suppurative exudate about the gasserian ganglion and in the sheaths of the several motor nerves of the eye.

3. Constant redness, swelling and hypersecretion of the nasopharyngeal tonsil and adjacent parts with an ascending otitis media.

4. The sphenoidal sinuses are constantly affected in all patients over 3 years of age. They were found markedly affected in twelve out of thirteen cases.

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10. Fraser and Comrie: Scottish Med. and Surg. Jour., 1907, xxi, 18.
11. Hübener and Kutscher: Deutsch. militär-arzt. Ztschr., 1907, xxxvi, 639.
12. Vagedes: Deutsch. militär-arzt. Ztschr., 1907, xxxvi, 647.
13. Westenhoeffer: Klin. Jahrb., 1906, xv, 657.

5. The antrum of Highmore is less often involved.

6. The ethmoidal sinuses are rarely and but slightly affected.

7. In all cases there is some swelling of the cervical lymph-nodes.

From these observations it seemed probable that there might be direct infection of the meninges from this nasopharyngeal focus through the sphenoidal sinuses. Especial emphasis is laid on the perihypophysial inflammation because of the close relation of the hypophysis to the sphenoidal sinuses and the known fact that in fetal life the sella turcica communicates with the throat through a hypophysial passage.

Two lymphatic paths are open for infection of the meninges from the nasopharyngeal process.

1. The infectious agent may make its way along the nerve sheaths, especially the several branches of the gasserian ganglion, as staphylococci, streptococci and typhoid bacilli have been shown by Homen to rise along the lymph channels of the sciatic nerve to the spinal cord. The inflammatory deposits surrounding these nerves are, however, readily shown to be secondary to the meningitis and descending, not ascending, processes.

2. The path of invasion may be along the carotid sheath to the region of the hypophysis.

However, investigation shows that the same perihypophysial inflammation is found in both otitic and tubercular meningitis. In the latter at least of these the infection undoubtedly reaches the meninges through the blood-stream and not by lymphatic channels. The value of the perihypophysial inflammation as evidence of the lymphatic transmission of the infection is therefore slight.

In the end Westenhoeffer admits the impossibility of proving the lymphatic transmission and assumes that the infection must reach the meninges through the blood-stream.

He even suggests that the whole throat affection may be secondary, although this seems improbable, inasmuch as it appears too early, in some cases before the onset of the meningitis, and also because the specific organisms are known to be often found in the throats of persons in good health (carriers).

Lymphatic transmission having apparently failed of proof, Westenhoeffer regards the infection as carried by the blood and probably by the arteries, inasmuch as no extensive thromboses are regularly present in cerebrospinal meningitis.

The cocci, as he says, are known frequently to be found in the blood, in some cases in the earliest stages of meningitis. In two or three cases lasting less than twenty-four hours, an endocarditis of the mitral valve and purulent myocarditis produced by the meningococci have been found.

Göppert[14] similarly summarizes his study of this question in these words:

> The whole respiratory tract, from the nose to the pulmonary alveoli, shows in the early stages of epidemic cerebrospinal meningitis more or less severe inflammatory changes. These may precede the onset. Chance brings one or the other—the pharyngitis, tonsillitis, pneumonia or bronchial catarrh, otitis media—of these conditions into the foreground. None of these affections is obligatory and therefore the opinion may be advanced that sometimes this, sometimes that point of the respiratory mucous membrane becomes the portal of entry of the meningococcus. Therewith must we accept the fact that the meningococcus may reach the brain through the blood channels, a conception which obtains support from the presence of the meningococcus in the blood.

Thus these two observers, disagreeing at the outset as to the importance of the local lesions of the respiratory tract, come in the end to agreement as to the probable route of infection of the meninges.

At this point the problem of demonstrating a meningococcus septicemia, either as an attendant feature of epidemic cerebrospinal meningitis or independently of it, becomes of great interest.

That the meningococcus may be found in the blood in certain cases of epidemic meningitis has been known for some time. Gwyn[15] first reported such a finding in a patient of Osler, and since then similar observations have been made by many others, Cochez and Lemaire,[16] Jakobitz,[17] Martini and Rohde,[18] Lenhartz,[19] Marcovitz,[20] Robinson[21] and Duval.[22] Elser,[23] in forty-one cases found the coccus in the blood in 10.25 per cent.; Dieudonné reports positive blood findings in four out of five cases, in one of which the nasal secretion was negative.

Especial interest, however, attaches to the presence of the meningococcus in the blood in patients free from meningitis. In 1908 I[24]

14. Göppert: Klin. Jahrb., 1906, xv, 527.
15. Gwyn: Bull. Johns Hopkins Hosp., 1899, x, 112.
16. Cochez and Lemaire: Baumgarten's Jahres., 1902, xviii. 91.
17. Jakobitz: München. med. Wchnschr., 1905, lii, 2178.
18. Martini and Rohde: Berl. klin. Wchnschr., xlii, 997.
19. Lenhartz: Deutsch. Arch. f. klin. Med., 1905, lxxxiv, 81.
20. Marcovitz: Wein. klin. Wchnschr., 1906. xix. 1312.
21. Robinson: Bull Ayer Clin. Lab., 1903, i-iii. 27.
22. Duval: Jour. Med. Research, 1908, xix, N. S. xiv, 258.
23. Elser: Jour. Med. Research, 1905, O. S. ix. 89.
24. Bovaird: Arch. Int. Med., 1909, iii. 267.

reported the case of a girl of 15 years who presented some of the symptoms of cerebrospinal meningitis, but whose spinal fluid remained free from meningococci, while the organisms were found in the blood. At that time I was able to find in the literature three other reports of meningococcus septicemia without meningitis, these being recorded by Salomon,[25] Liebermeister[26] and Andrewes.[27] Netter has since recorded the case of a woman suffering from diarrhea, fever and general malaise, whose blood agglutinated two strains of meningococci, but whose blood culture was not taken. The patient's sister had cerebrospinal meningitis at the time.

Cecil and Soper[28] have collected from literature four cases of meningococcus endocarditis, two of these being the cases of Westenhoeffer already referred to, and add an observation of their own. The patients of Warfield and Walker[29] and Cecil and Soper gave no evidences of meningitis.

The occurrence of meningococcus septicemia both in conjunction with the cerebrospinal meningitis and independently of it, lends support to the view that the infection of the meninges is brought about through the blood, the primary focus being in the respiratory tract.

Elser and Huntoon[30] summarize the evidence of hematogenous infection in these words:

> The early appearance of the meningococcus in the blood in a considerable number of cases, the appearance of general sepsis suggested by some patients early in the disease, the lesions in parts far removed from the central nervous system found at autopsy of individuals who succumbed to the disease within twenty-four hours of its inception, and finally the appearance of characteristic lesions in the eye synchronously with manifestations referable to the central nervous system, all point to an early generalization of the meningococci, but are not competent to prove that such an infection antedated the meningeal involvement.

The experimental study of this problem has not yet yielded decisive results. Bettencourt and Franca[6] failed to produce meningitis in monkeys either by rubbing cultures of the meningococcus into the nasal mucous membrane or by intravenous injection.

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25. Salomon: Berl. klin. Wchnschr., 1902, xxxix, 1045.
26. Liebermeister: München. med. Wchnschr., 1908, lv, 1978.
27. Andrewes: Lancet, Lond., 1906, lxxxiv-ii, 1172.
28. Cecil and Soper: Arch. Int. Med., 1911, viii, 1.
29. Warfield and Walker: Bull. Ayer Clin. Lab., 1903-6, i-iii, 81.
30. Elser and Huntoon: Jour. Med. Research, 1909, xx, 373.

Flexner[31] succeeded in producing meningitis in monkeys by intraspinal injection, the resulting meningitis having in this case also the basal distribution thought suggestive of nasopharyngeal infection.

Elser and Huntoon, by intravenous injections of *Streptococcus mucosus* in rabbits succeeded in producing a meningitis which in its onset and the distribution of lesions resembled the meningococcus meningitis of man.

Finally, we may say that the evidence at our command at present strongly suggests that the primary infection in epidemic cerebrospinal meningitis is respiratory, in most cases nasopharyngeal, and that the meningeal infection is developed through the blood.

Protection of the community therefore will demand not only the isolation of those sick with the epidemic disease, but the detection of the many unaffected "carriers." To what extent this may be practicable remains to be seen. In the restricted fields offered by regimental organizations, the German military officers have already applied these methods with apparent success.

The efforts to free carriers from their infection (nasopharyngeal) have, so far as I can learn, proved ineffective. Various applications, douches and insufflations have been tried without success. In this regard the experience seems to repeat that with diphtheritic infections of the throat. In time the infection appears to die out in most cases, but treatment does not hasten that desired end.

Our present knowledge would suggest the desirability of treating these persons by serum or vaccines. The possibility of protecting the exposed by like means naturally presents itself, but thus far I have not been able to learn of any work along these lines.

137 East Sixtieth Street.

31. Flexner: Jour. Exper. Med., 1907, ix, 142.

THE SIGNIFICANCE OF THE PYLORIC REFLEX IN TRUE AND PSUEDOPYLORIC STENOSIS IN INFANTS

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The following case study is presented with the hope that it may illustrate how a regard for the opening pyloric reflexes may serve us in the medical cure of pyloric stenosis and pyloric spasm in young infants.

Methods used in the treatment of the present case are in no way new. It has been known for a long time that lavage and the antacids have been useful and effective in the treatment of these conditions and the explanation for their beneficial effects have been well interpreted. There are, however, a few principles which may be said to be comparatively new which are not generally considered and which make the interpretation of our previous success with these methods still more clear. These are the factors which govern the opening and closing of the pylorus. While we have no definite comparative experiments to prove it, it might well be argued on clinical grounds that in the condition of hyperchlorhydria, accompanying a hypertrophic stenosis of the pylorus or a stenosis from any other cause, in that stage of the disease when spasm can be demonstrated, the irritated tissues respond more markedly to the reflex stimuli. We should at least be able to demonstrate in a stenosis which is not complete, yet of marked degree, whether or not the reflex mechanism is still intact.

We have seen experimentally in the normal infant's stomach[1] how an antacid may be employed to keep the pylorus closed and thus impede the passage of chyme from the stomach by its action in delaying the opening reflex. Under certain conditions a paradoxical reaction may be said to take place; that is, an antacid may be employed to facilitate or expedite the passage of chyme from the stomach. When, for example, an antacid is added in proper amount to a hyperacid stomach, instead of delaying the opening reflex, as is the case in the normal stomach in which achlorhydria is the rule, the opening reflex is brought into play and kept in activity by an early series of short duodenal closings, brought about by

1. Cowie and Lyon: Am. Jour. Dis. Child., 1911, ii, 252.

the antacid overcoming the excess of acidity or delaying its rapid appearance. Thus, during the first part of digestion one could expect the stomach to empty itself quickly; during the latter part when the acidity has reached its height, more slowly. The question of whether or not we are dealing with a hypersecretion or a simple hyperchlorhydria is at this point of particular importance and should be determined. In the former condition the continuous flow of gastric juice leaves in an otherwise empty stomach an acid fluid, which, if neutralized before the meal enters, would, theoretically, facilitate at least a second or a third pyloric opening. With an antacid duodenum a pyloric opening should come as soon as the acidity of the chyme reaches a certain point and that point we have shown, in the infant, is before the appearance of free acid. When free acid appears the duodenal closing is prolonged, depending on the ability of the duodenum to dissipate its acquired acidity. Hence, as stated before, we might expect a lower stomach motility or propulsion force during the latter part of digestion.

In the consideration of the subject of infantile pyloric stenosis I must necessarily confine myself to that group of cases in which hyperchlorhydria plays an important part, for it is with this group alone that I have had experience. A word may be said at this point. It is my belief that a very much larger per cent. of the cases of infantile pyloric stenosis and pseudo-stenosis is associated with hyperchlorhydria than is usually conceded. I form this belief not from a large experience with the disease in infants, as I have thus far seen but six cases, but from data which I have gathered during a long and somewhat careful experience in the observation of hyperchlorhydria in the adult, and of stomach analyses in infants and children. Such observations disclose that stomach vagaries are alike not uncommon in infants, young children and adults. The same food stimulus while it calls forth an equal amount of juice to saturate it each time it is placed in the stomach, yet the stomach may differ in its response, as indicated by the degree of acidity, within very wide limits from day to day. Although in the adult this fact was early pointed out by Ewald, only comparatively recently has it been taken into consideration in the diagnosis and treatment of stomach states. It has not been taken into account in many of the cases of infantile pyloric stenosis recorded as cases of achlorhydria. In all of the cases I have seen there have been times when no test for free acid could be obtained. I made the statement some years ago, and it may not be out of place to repeat it here, that a single observation of the stomach juice is of no more signifi-

cance in the diagnosis of stomach disease than a single observation of a thermometer in the diagnosis of a fever. Spasm of the pylorus does occur with achlorhydria in adults and in infants. It has been my privilege to see a number of cases among adults, and in one carefully studied case, which I should like to record, actually to see the spasm occur twice during laparotomy, a pyloroplasty by Professor Darling and myself. Immediately following the tight contraction of the pylorus, which become as hard as a piece of India rubber, the peristaltic waves of the stomach brought the organ almost completely out of the abdominal wound. It receded and after a short interval went through a similar but less marked phase.

CASE REPORT

History.—Sept. 29, 1910. Robert L. Born Aug. 1. 1910; normal birth. Well developed boy weighing nine pounds. Bottle fed from birth. The initial loss of weight was regained in fourteen days. The infant seemed to be developing normally, with the exception of few and hard stools, until August 14, when he first vomited. He had been fed on a formula of milk and milk-sugar obtained from the milk-sugar package. He was now put on condensed milk. The vomiting continued whenever food was given, often in large amounts. The vomitus was frequently "very sour." The vomiting seems to have been allayed for short periods. He retained malted milk feedings at one time for four or five days, and another similar food for one week. Vomiting, however, recurred and wet nursing was tried for ten days; the vomiting, however, persisted. Various other "methods" of feeding were tried but from the fourteenth day of life the infant continued to lose progressively in weight with the report September 29 that it had had but two natural bowel movements since birth. September 27 the patient had what was called a "sinking spell." There was marked stupor and general relaxation of the body which lasted a few minutes and was apparently overcome by whiskey. The infant now vomited everything that was put into its stomach. The bowel movements were very infrequent, very small, dry, dark green, with no curds.

Family history negative. Two other children normal.

Examination.—When first seen by me Sept. 29, 1910, the infant was much emaciated, the skin hung in folds over the extremities and its elasticity was practically absent. There was no panniculus. The skeleton was well formed. Fontanels normal. Muscles extremely wasted. No enlarged lymph-nodes. Mucous membranes were somewhat reddened. The lips were dry. The thymus could not be satisfactorily outlined. Thyroid negative. Thorax negative. The general appearance was that of a case of marked "atrophy."

The abdomen was scaphoid in appearance, fuller in the epigastrium than below the navel. On first examination there was a suggestion of peristalsis high in the epigastrium, but not positive. A hard mass about 2.5 cm. in diameter was grasped between the fingers 4 cm. above the navel and a little to the right. It was smooth and felt like an hypertrophied pylorus. There was no pitting on pressure. I failed to find the mass on subsequent examinations. Distinct but small peristaltic waves were observed high in the epigastrium on several occasions but careful watching did not enable me to see the wave pass progressively from left to right. There was distinct separation of the recti abdominalis down to two fingers below the umbilicus.

TABLE 1.—STOMACH ANALYSIS

Observation No.	Date	Amount Fed, c.c.	Interval Since Last Feeding, Hr. Min.	Amount Recovered, c.c.	Excess of Amt. Fed, c.c.	Condition of Stomach Before Feeding	HCl	Total Acid	$NaHCO_3$ with Feeding, gm.	Remarks
	1910									
1	9/29	45	3:00	45	0	.....	8	24	0.0	Sustained duodenal closing reflex.
2	9/30	45	3:00	56	11	.....	20	56	0.0	Sustained duodenal closing reflex.
3	*	45	3:00	53	8	3 hours prev., empty.	20	52	0.0	Sustained duodenal closing reflex.
4	.....	45	3:00	0	0	Empty	..	..	2.5	Released duodenal closing reflex.
5	10/ 1	45	3:00	0	0	.....	..	..	2.5	Released duodenal closing reflex.
6	.....	60	3:00	0	0	.....	..	..	2.5	Released duodenal closing reflex.
7	10/ 2	60	3:00	35	0	.....	20	62	0.0	Sustained duodenal closing reflex.
8	.....	60	3:00	58	0	Vomit. large amt.	18	52	0.0	Sustained duodenal closing reflex.
9	10/ 3	60	3:00	74	14	Four feedgs. since lavage	20	60	0.0	Sustained duodenal closing reflex.
10	.....	60	3:00	30	0	Empty	0	20	2.5	Delayed pyloric opening reflex.
11	10/ 4	60	3:00	0	0	.....	..	..	0.0	.....
12	10/ 5	60	3:00	36	0	.....	12	60	0.0	Sustained duodenal closing reflex.
13	10/ 6	60	3:00	130	70	Vomit. large amt. during night.	18	58	0.0	Sustained duodenal closing reflex.
14	10/ 7	60	3:00	0	0	Previous feed 2.5 gm. carb.	+	—	0.0	.....
15	10/ 8	60	3:00	0	0	.....	..	..	2.5	.....
16	10/ 9	60	3:30	14	0	.....	0	12	0.0	Delayed pyloric opening reflex.
17	10/10	60	3:30	15	0	2.5 gm. carb. previous meal.	..	..	0.0	.....
18	10/11	60	3:30	4	0	.....	22	45	2.5	Released duodenal closing reflex.
19	10/12	60	3:30	0	0	.....	..	..	0.0	.....
20	10/13	60	3:30	0	0	2.5 gm. carb. previous meal.	..	..	0.0	.....
21	10/17	60	3:30	11	0	.....	..	..	0.0	.....
22	10/25	60	3:30	0	0	.....	..	..	0.0	.....
23	10/26	60	3:30	0	0	.....	..	..	0.0	.....
24	11/29	98	3:30	13	0	.....	48	88	0.0	Sustained duodenal closing reflex.
25	11/30	98	3:30	5	0	.....	..	..	0.0	.....
26	12/ 1	98	3:40	0	0	.....	..	..	0.0	.....
27	12/ 2	98	3:40	12	0	.....	40	..	0.0	.....
28	12/ 3	98	3:40	0	0	.....	..	..	0.0	.....
29	12/ 7	120	4:00	2	0	.....	..	..	0.0	.....
30	12/10	120	4:00	3	0	.....	..	..	0.0	.....
31	12/13	120	4:00	0	0	.....	..	..	0 0	.....
	1911									
32	2/27	150	4:00	1	0	.....	++	..	0.0	.....
33	3/23	158	3:00	6	0	.....	10	..	0.0	.....

*Time of Observation 2, 10 a. m.; 3, 1 p. m.; 4, 4:15 p. m.; 5, 11 a. m.; 6, 5 p. m.; 7, 12 m.; 8, 6 p. m.

Stomach Examinations.—(See Table 1.)

Urine Examination.—(See Table 2.)

Feeding Record.—September 29 to October 3 plain whey. October 3 a small amount of cream was added making the formula approximately a 0.4 per cent. fat, 5 per cent. sugar, 1 per cent. protein; to this enough sodium citrate was added to prevent calcium para-casein curds. The strength of the food was gradually increased. Nov. 2 he was getting 1.2 per cent. fat, 5 per cent. sugar, 1.6 per cent. protein. From now on the whey was gradually replaced with water and completely discontinued December 4, at which time he was getting 2 per cent. fat, 5 per cent. sugar and 1.6 per cent. protein. The fat per cent. was increased December 6, 3 per cent. fat, 5 per cent. sugar, 1.6 per cent. protein; January 15, 3 per cent. fat, 5 per cent. sugar, 2 per cent. protein. Citrate of soda was discontinued March 8, 1911. Whole milk was reached Oct. 8, 1911.

Weight Record.—(See Charts 1 and 2.)[2] September 30 the infant weighed 6 pounds 8 ounces. The total loss of weight during observation was 8 ounces. From the end of the first month on there was a steady gain in weight. The ratio increasing in proportion to the proximity of the food line to the energy line. The birth weight was reached March 22 (Fig. 1), seven months, twenty-two days after birth. The child's development is now perfect and he ranks if anything in advance of babies of his age.

DISCUSSION OF CASE

Owing to loss of the nurse's temperature record for the first seven days I am unable to give a true curve of the temperature during that time. The dotted line in the temperature curve, Chart 2, I have improvised. The patient came under treatment with a sub-normal temperature. This continued until the second day of the administration of sodium bicarbonate, when the temperature was slightly above the normal line, and rose to 101 F. the following evening, after which it gradually declined to subnormal. Accurate temperature records begin October 6, and are represented by solid black. Subnormal temperature had been frequently noted before I saw the patient. The third and fourth days after beginning the sodium bicarbonate the fever developed. The following day I suspected I was dealing with a salt fever resulting from the sodium chlorid formed from the action of the stomach acid on the sodium salt. The $NaHCO_3$ was discontinued for two and one-half days as a control. The temperature dropped and followed the subnormal type, which will be seen was the characteristic temperature curve of this patient, and which continued to be.

October 7 the sodium bicarbonate was resumed. It was followed by a quite prompt pyrogenic reaction; but although the drug was continued

2. This record does not appear on the charts. It was lost with the records before referred to. October 8 I find a note saying the baby has lost 4 ounces since last weight.

the temperature curve was irregular, at times subnormal, at other times hypernormal. The dose was increased so that on October 12 as much as 8.71 grams of sodium chlorid would result from the complete action of hydrochloric acid on the sodium bicarbonate given. A marked pyrogenic reaction, 102.2 F., developed along with the formation of this large amount of salt and continued through the following day, during the latter part of which the sodium bicarbonate was discontinued. From now on no carbonate was given and the characteristic subnormal temperature curve was resumed. Synchronous with the temperature rise there was a marked edema of the extremities (water retention), increase

TABLE 2.—URINE EXAMINATIONS

Date of Sample	Color, Etc.	Reaction	Specific Gravity	Albumin	Sugar	Acetone	Diacetic Acid	Sediment
1910								
10/ 3	Yellow	Alk. +	1.026	0	0	0	0	Negative.
6	Yellow	Alk. +	.....	0	0	++	0	A few large and small hyaline casts.
14	.....	Alk. +	1,028	0	0	0	0	More similar casts than before. Not large numbers.
17	Pale	Alk.	1.010	0	0	—	—	A few hyaline and epithelial casts.
21	Pale	Acid	1.007	0	0	—	—	An occasional hyaline cast.
24	Pale	Alk.	1.005	0	0	—	—	Negative.
26	Pale	Alk.	.....	0	0	—	—	Negative.
11/ 1	Pale	Alk.	.....	0	0	—	—	Negative.
12/13	Pale	Alk.	1,011	0	0	—	—	A few hyaline and granular casts.
1911								
2/13	Pale	Acid	1.000	0	0	—	—	Negative.

in weight and frequent stools, all of which subsided after discontinuing the sodium salt. It will be further observed that during the period of alkali administration free acid appeared in the stomach (Chart 2, and Table 1). There can hardly be any question but that the sodium bicarbonate was completely changed by the acid of the gastric juice. The figures below the temperature curve, Chart 2, show the number of grams of sodium chlorid formed in the stomach. Chart 3 records the total daily amount of alkali given. We have here a marked instance of a salt fever brought about by the administration of a salt, which, when given normal babies at one dose to the amount of 4 grams, produces no pyrogenic

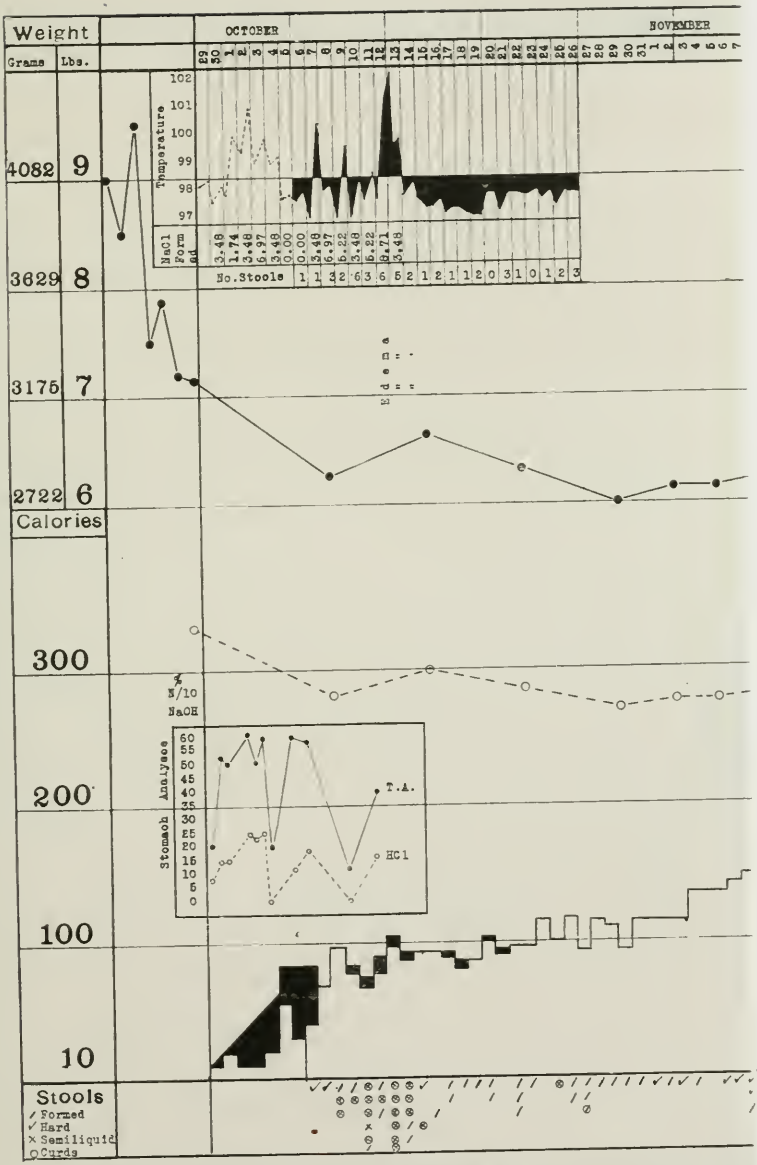


Chart 2.—Temperature curve shows a salt fever. Below the curve weight. Dotted line, energy line, indicating caloric requirements. Belo indicates the amount of food vomited, the light portion the amount

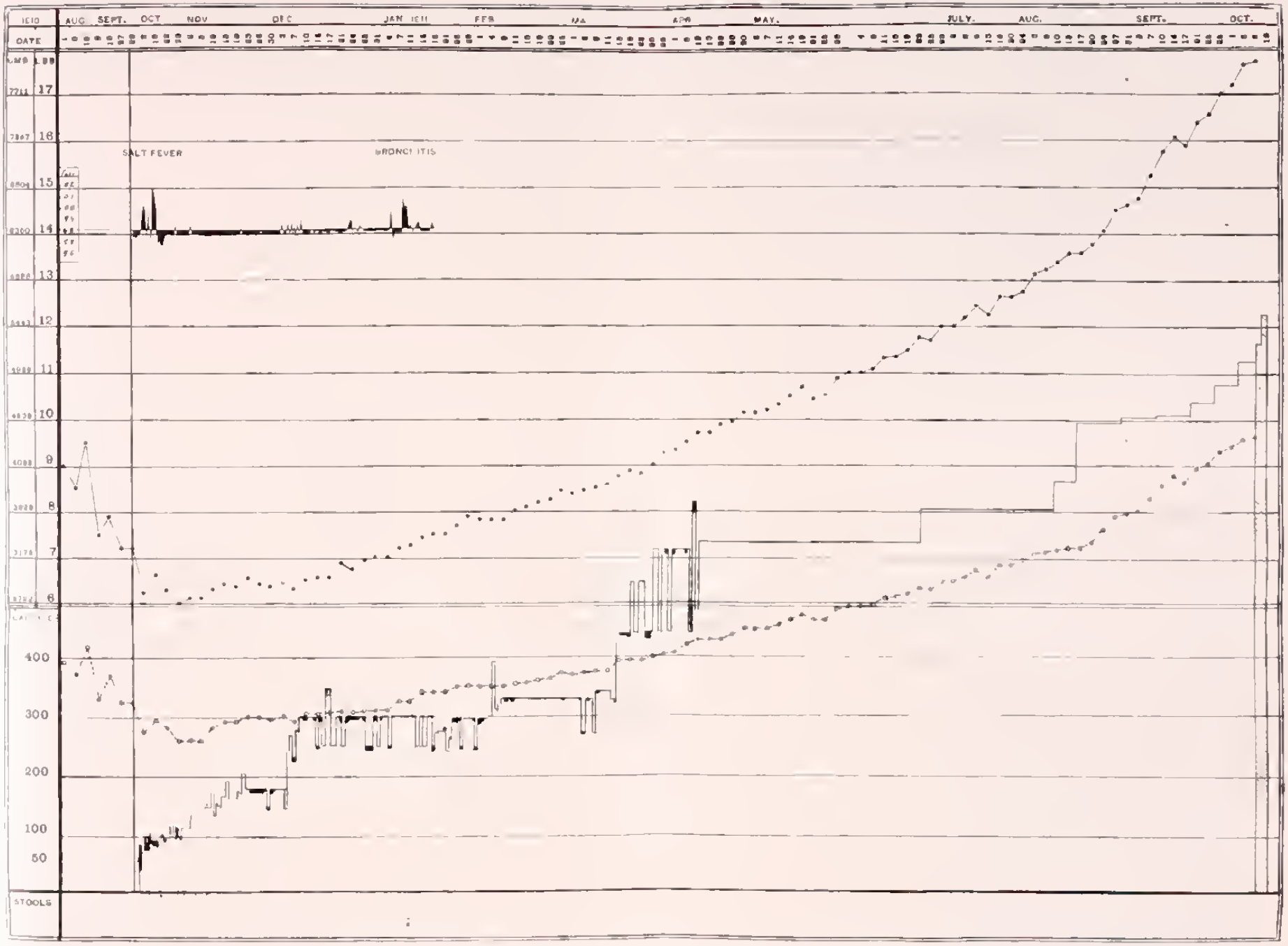


Chart 1.—This chart gives the weights from birth to one year, two months. The dotted line is the energy line. The food blocks start below the energy line. The dark part indicates the amount of food vomited, the white part the amount retained. The weight begins to rise as the food approaches the energy line.

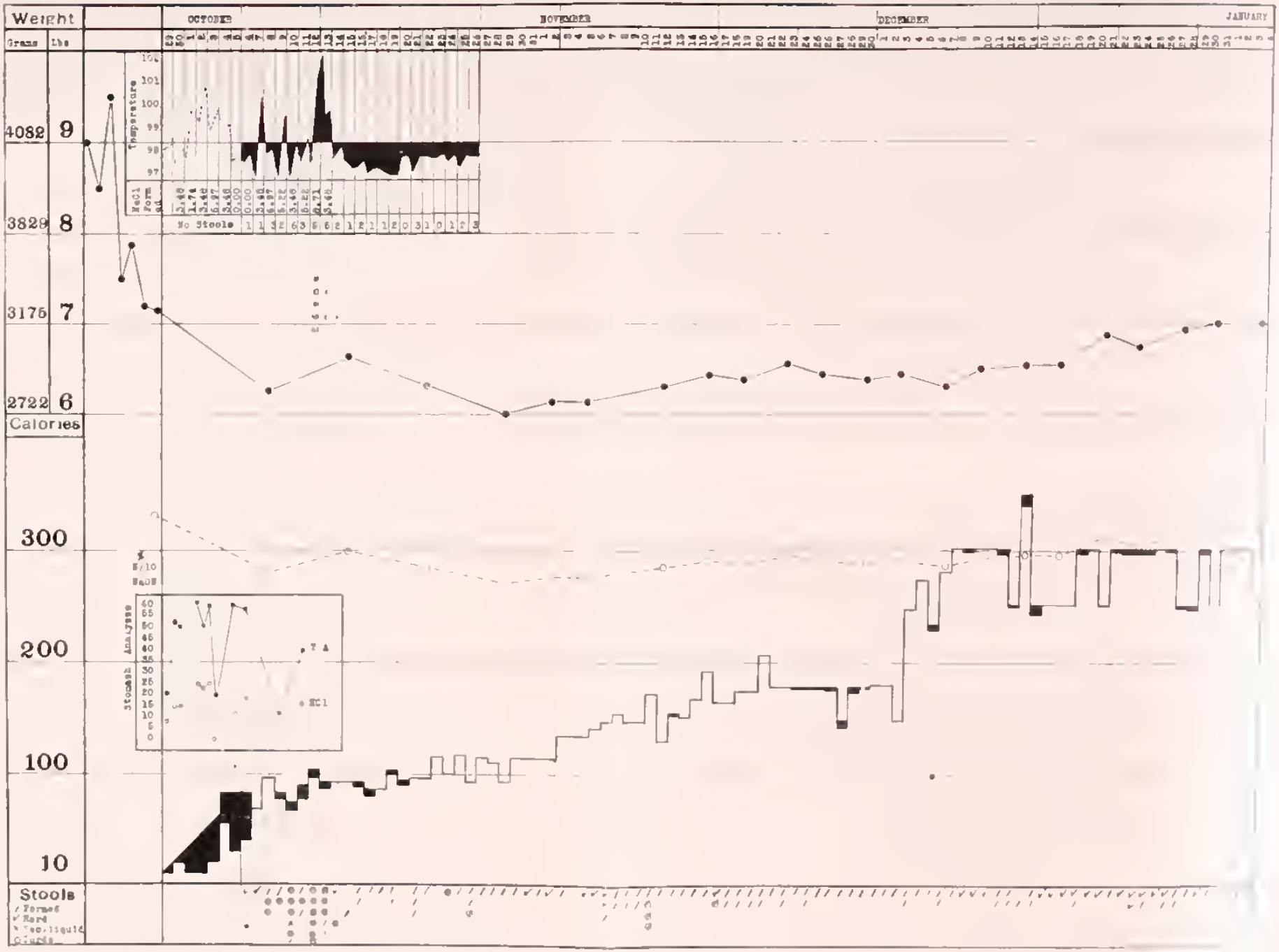
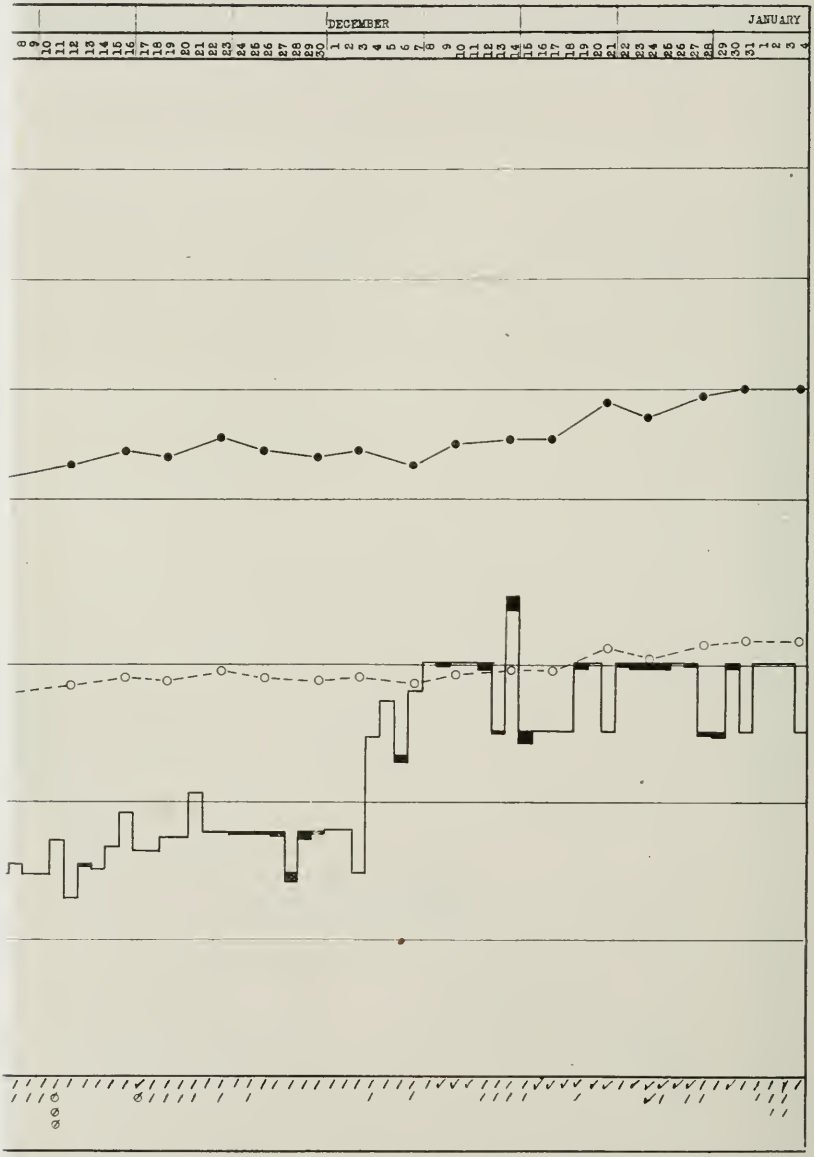


Chart 2.—Temperature curve shows a salt fever. Below the curve the number of grams NaCl formed from the NaHCO in stomach. Solid line, weight. Dotted line, energy line indicating calorie requirements. Below the calories of food given and retained are indicated. The black portion indicates the amount of food vomited, the light portion the amount retained.



the number of grams NaCl formed from the $NaHCO_3$ in stomach. Solid line. w. the calories of food given and retained are indicated. The black portion retained.

reaction.[3] The patient was getting full whey as food. It might be argued that the whey salts had something to do with the pyrogenic reaction. However, whey continued to be the bulk of the food until November 2 and was not completely discontinued until December 6. Throughout this entire period the subnormal type of temperature predominated, a febrile reaction occurring only during an attack of bronchitis, as shown on Chart 1.

The action of the alkali on the pyloric reflex. In Table 4 in the column devoted to remarks, I have given an interpretation of the conditions found in the stomach at the time of the observation and of the happenings prior to the introduction of the stomach tube. I believe Observations 1, 2, 3, 7, 8, 9, 12 and 13 are reliable illustrations of sustained duodenal closing of the pylorus; Observations 4, 5, 6 and 18, illustrations of released duodenal closing brought about by the alkali, and Observations 11 and 13, illustrations of delayed pyloric opening.

We have shown experimentally how the opening of the pylorus may be delayed in a normal infant by giving it an alkali in its food. A similar result might follow the administration of too much alkali in an infant with hyperchlorhydria. Hence the importance of regulating the dose of acid by means of stomach analyses. We may fail in our treatment of pyloric stenosis and spasm by giving too much or too little antacid. One may unwittingly do damage to the organism by the use of antacids by the development of a fever, edema and diarrhea, not suspecting the antacid to be at the bottom of it all.

I think there can be no question that in the present case the rather quick and sure benefit came from the controlled use of the alkali. In six days from the beginning of treatment over two-thirds of the amount given was retained, and on the ninth day the total amount given was retained. See Chart 3.

September 30. Three carefully planned observations followed each other successively (Observation 2). At 10 a. m., three hours after 45 c.c. of whey, 56 c.c. were recovered; the stomach was carefully washed and drained and 45 c.c. of whey given. At 1 p. m. (Observation 3), three hours later, 53 c.c. were recovered. This represented the 45 c.c. of food and 8 c.c. of secretion. These two tests showed that absolutely nothing had passed the pylorus in six hours. The stomach was again drained and (Observation 4) 45 c.c. of whey and 2.5 grams of sodium bicarbonate

3. Cowie, D. M.: Am. Jour. Dis. Child., 1912, iv.

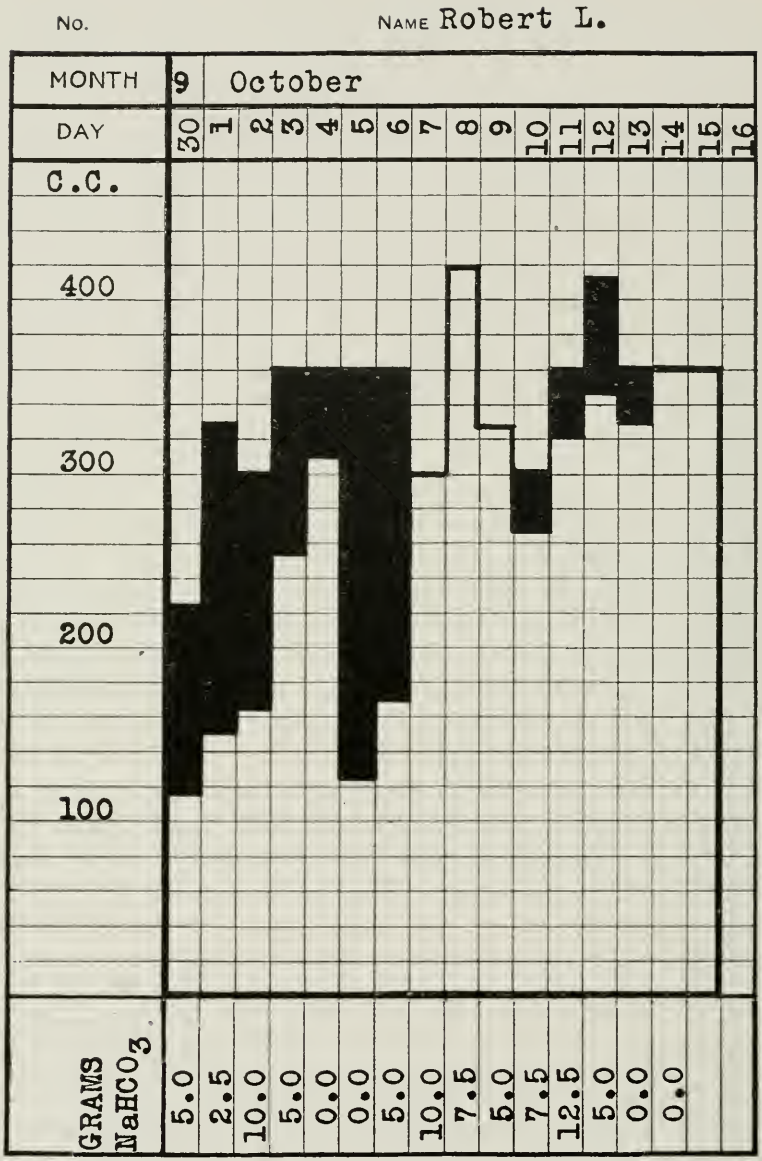


Chart 3.—Showing the amount of food and total daily amount of sodium bicarbonate given during the first sixteen days of treatment. Black indicates the number of c.c. vomited.

were given. At 4:15 p. m., three hours later, the stomach was completely empty. The duodenal closing reflex having been released. (All feedings given gavage.)

From the standpoint of vomiting and emaciation the case was a marked one. For several days before treatment was begun apparently nothing passed the pylorus. Citrate of soda was added to the food as soon as milk was given. Its effect was uniform in making it possible for us to control the size of the curd, and to recover in most instances the entire stomach contents.

The Urine (Table 2).—As only one urine examination was made prior to the administration of the alkali it cannot positively be said that it or the resulting salt fever was the exciting cause of the casts. However, the only time casts occurred in sufficient numbers to cause concern, was the day following the highest temperatures recorded, October 14. By October 26 the urine was free from casts. A few were found December 13. Albumin tests were always negative. The records in Table 2 show that more careful routine examinations would be of value in such cases.

High Milk Protein Feeding.—Red meat protein is the strongest stimulant for the gastric acid secretion of which we know. Milk protein, on the other hand, stimulates the flow of acid much less markedly and has an enormous binding power for acid. With this fact in mind, it was my desire at the outset to discontinue the alkali as soon as possible and replace it with a high protein mixture. Satisfied, however, with my success and remembering that wisdom is the better part of valor, I cautiously reached 1.6 per cent., November 2, and 2 per cent. January 15, three months after beginning treatment. From now on the gain was marked and the regurgitation less marked. Theoretically, high milk protein combined in such a way as to prevent large curd formation in the stomach would be advisable in cases of spasm or stenosis with hyperchlorhydria. The effect of high protein on the kidney epithelium should not be forgotten. It should be remembered that high fat food tends to slow stomach evacuation as the duodenal closing reflex has been shown to be excited by fat in the duodenum.

Stomach Washings.—The object of the study of this case as stated before was to determine how much a regard for the opening and closing reflex could serve us in overcoming pyloric spasm. I think we are all agreed that in these cases associated with hyperchlorhydria, spasm is

always present. To this end I endeavored, in so far as was feasible, to exclude stomach washings. Accordingly thorough lavage was resorted to a very few times. The tube nevertheless was passed at frequent intervals to determine the evacuation rate of the stomach. After expressing the contents a bulbful of water was washed through to assure us that all had been recovered. After the first few days this was done once a day or once in two days for a number of weeks and doubtless it had a beneficial effect. Just preceding the present case I treated a severe case by thorough stomach washings before each meal, six times daily. The patient made almost equally as good progress, but the necessary care was almost unendurable for the skillful mother and nurse. By this method we were assured of at least two opening reflexes. The first before the chyme contained free acid, and the second because the acquired duodenal acidity was probably normal and was normally overcome. In this latter case for some time after beginning the treatment we always recovered greater or smaller amounts of food at the end of the four-hour period. I am sure if we bear this reflex action in mind we shall have more uniform success in the care of our cases. Cure ultimately means that we have produced conditions favorable to normal pyloric function.

A GRAPHIC CHART METHOD OF STUDYING AND TEACHING THE PRINCIPLES OF INFANT FEEDING

WITH SPECIAL REFERENCE TO THE IMPORTANCE OF THE ENERGY LINE *

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I wish to present a method which I have been using with considerable satisfaction in teaching the principles of infantile nutrition, a graphic chart method which supplements previous instruction. The chart is simple, easily understood and records the weight variations, the energy line, which indicates how much food the infant needs, the food blocks, which show how much food has been given and retained, and presents a graphic representation of the number and character of the stools. Various other happenings of the day can also be indicated. Thus the chart forms a complete summary of the case for each day. A few explanations will be necessary.

The chart is arranged for daily records for eight weeks with room for a gain of 4 pounds. The spaces between the ordinates represent days, each abscissa represents 2 ounces, between the abscissæ 1 ounce. A gram column parallels the pound column. The calorie column may be started with each abscissa representing either 10 or 20 calories and is usually begun on an even number approximately corresponding to the caloric requirement 1 pound below the entrance weight, in order to allow for weight drops, etc.

Plotting the Energy Line.—This line is constructed from the infant's weight, 45 calories per pound during the first six months of life, gradually declining to 40 or 36 calories during the latter months of the first year.

Plotting the Food Line.—The caloric value of the food is calculated in the usual way. After the student has become thoroughly familiar with this computation he is given a table of the caloric values of one ounce of the various foods used in the ward. (Table 1.) The amount of food in calories ingested and retained is charted. (See Chart 9.)

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*From the Department of Pediatrics, University of Michigan.

TABLE 1.—THE CALORIC VALUE OF ONE OUNCE OF THE VARIOUS MODIFIED MILK FORMULÆ AND FOODS USED IN PALMER MEMORIAL WARD

Formula, Per Cent.			Calories From			
F	S	P	Fat	Sugar	Protein	Total
1	5	0.5	2.79	6.15	0.61	9.55
1.5	5	0.5	4.18	6.15	0.61	10.95
1.5	5	0.75	4.18	6.15	0.922	11.235
1.5	5	1	4.18	6.15	1.23	11.56
1.5	5	1.5	4.18	6.15	1.845	12.17
1.5	5	2	4.18	6.15	2.46	12.79
2	5	0.5	5.58	6.15	0.615	12.34
2	5	0.75	5.58	6.15	0.922	12.05
2	5	1	5.58	6.15	1.23	12.96
2	5	1.5	5.58	6.15	1.84	13.57
2	5	2	5.58	6.15	2.46	14.19
2.5	5	1	6.97	6.15	1.23	14.35
2.5	5	1.5	6.97	6.15	1.84	14.96
2.5	5	2	6.97	6.15	2.46	15.58
3	5	1	8.37	6.15	1.23	15.75
3	5	1.5	8.37	6.15	1.84	16.36
3	5	2	8.37	6.15	2.46	16.98
3	6	1	8.37	7.38	1.23	16.98
3	6	1.5	8.37	7.38	1.84	17.59
3	6	2	8.37	7.38	2.46	18.21
3	5	2.5	8.37	6.15	3.07	17.59
3	5	3	8.37	6.15	3.69	18.21
3.5	5	3	9.76	6.15	3.69	19.60
4	5	3	11.16	6.15	3.69	21.01

Whole milk	21.01
Milk Sugar	13.00
Cow's milk	21.01
Woman's milk	20.5
Skim milk	12.0
Whey	6.0
Buttermilk, approximately	5.0
Precipitated casein, approximately	15.0
Eiweissmilk, approximately	11.0*
Keller's malt-soup, approximately	24.0
Oat flakes, dry, approximately	116.0
Barley flour, dry, approximately	103.0

*The caloric value of *Eiweissmilch* varies 11 and 15 calories per ounce, depending on the percentage of fat in the whole milk and the quality of the buttermilk.

Charting the Stools.—A series of symbols are used. These may be varied as one desires. The usual ones employed and which the nurses and students use with readiness are the ones indicated in the stool column.

Of the combination of characters below the first indicates a hard stool with curds; alkaline in reaction; the second a liquid stool with curds, mucus and blood; acid reaction; the third an extra sign for any other type of stool.

The chart when completed for the day is a representation of the so-called percentage and caloric methods, both of which must figure in the proper feeding of an infant. There has been so much said about the advantages of one method over the other that I usually begin my work in infant feeding by illustrating the foundation that has been laid in this country by American masters whose names are so familiar to all of us. America has been in no way behind in the development of a knowledge of infantile nutrition. Chart 1 illustrates how closely we have come to the needs of the body as attested by the energy line. I have plotted the

TABLE 2.—PROTEIN REQUIREMENTS PER KILO OF BODY-WEIGHT

Age	Required Grams of Protein per		
	Kg. Body-Wght	Pound	Ounce
2 Weeks	1.5	0.68	0.0425
2 Weeks	1.5	0.68	0.0425
3	2.0	0.90	0.056
4	2.5	1.10	0.0687
2 to 12 months ..	2.5-3.3	1.10-1.5	0.093

weight-curve of a normal bottle-fed baby (taken from Holt) and the maximum amount of food in calories used as a routine by those who follow the percentage feeding scheme. (Arranged from Holt's table.) The gain in weight is seen to follow feeding above the energy line. A chart plotted with the optimum amount of food generally prescribed would bring the food line from 20 to 70 calories above the energy line. It will be seen that infants fed by this scheme have not been underfed, and it should also be stated that the proportion of each food constituent has been carefully adjusted.

The most important point to impress on the student is the basic protein requirement of the body. By a previous special study of metabolism as related to infantile growth and development, the student has

TABLE 3.—CHART MAKING EXERCISE, BABY A., CASE 1

Date	Weights from Birth		Food from Birth		Stools from Birth
	Pounds	Ounces	Formula	Ounces	
June 1	7	10	.....	..	2 normal
2	..	...	.....	..	2
3	7	8	.....	..	3
4	..	...	6% sugar whey	10	3
5	..	...	.....	..	4
6	7	5	.....	..	3
7	..	...	1½-5-½	20	3
8	..	...	.....	..	1 normal, 1 curd
9	7	8	.....	..	2 normal
10	..	...	.....	..	3
11	7	10	.....	..	2
12	..	...	.....	..	2
13	7	11	.....	..	3
14	..	...	2-5-¾	30	3
15	..	...	.....	..	3
16	7	14	.....	..	2 normal, 1 with curds
17	..	...	.....	..	3 normal
18	8	...	.....	..	3
19	..	...	.....	..	2
20	8	4	.....	..	4
21	..	...	.....	..	2
22	..	...	.....	..	2
23	..	...	.....	..	2
24	8	6	2-5-1	30	2
25	..	...	.....	..	2
26	..	...	.....	..	2
27	8	10	.....	..	3 normal, 1 with curds
28	..	...	.....	..	3
29	..	...	....	..	2
30	..	...	.....	..	2
July 1	8	14	.....	..	2
2	..	...	.....	..	2
3	..	..	.....	..	2
4	8	14	.....	..	1
5	..	...	2½-6-1	31	1
6	..	...	.....	..	3 normal, 3 with curds
7	8	14	.....	..	2 normal, 1 liquid curds
8	..	...	.....	..	3 with curds
9	..	...	.....	..	2 curd, 1 liquid, with curds
10	8	12	.....	..	2 4
11	..	...	.....	..	6 liquid with curds
12	8	8	.....	27	4
13	..	...	.....	..	3
14	..	...	.....	..	2 with curds, 1 normal
15	8	10	.....	..	3 normal
16	..	...	.....	..	2
17	..	...	.....	..	2
18	9	2	.....	28	3
19	..	...	.....	..	3
20	..	...	.....	..	2
21	9	6	.....	..	2
22	..	...	.....	..	3
23	..	...	.....	30	3
24	9	10	.....	..	2
25	..	...	.....	..	2
26	..	...	.....	..	2

TABLE 4.—CHART MAKING EXERCISE, BABY B., CASE 2

Date		Weights		Temperature		Food		Stools
		Pds.	Ounces	M	E	Formula	Ounces	
July	21	12	12	98.4	98.8	3-6-1½	36	2 normal
	22	..	..	98.	98.6	.....	....	2 normal
	23	..	..	98.2	98.4	.....	....	3 normal
	24	13	..	97.8	98.4	.....	....	2 normal
	25	..	..	98.4	99.	.....	....	3 normal
	26	..	..	98.6	98.6	.....	....	2 normal
	27	13	4	98.4	98.8	.....	....	2 normal
	28	..	..	98.	98.6	.....	....	1 normal, 1 liquid
	29	13	5	98.8	98.4	.....	....	2 liquid, acid
	30	..	..	98.6	99.	.....	....	2 semi-liquid, mushy
	31	..	..	98.	98 8	.....	....	1 semi-liquid, 1 normal
August	1	13	5	98.6	98.8	.....	....	2 normal
	2	..	..	98.	98.6	.....	....	2 hard
	3	13	4	98.4	98.6	.....	....	3 semi-liquid, mushy
	4	..	..	98.	98.9	.....	....	4 semi-liquid, mushy
	5	13	4	98.4	98.8	.....	....	4 semi-liquid, mushy
	6	13	6	98.8	98.6	.....	....	5 semi-liquid, mushy
	7	13	1	98.6	98.4	.....	31½	3 semi-liquid, mushy
	8	12	11	97.6	98.6	.....	....	3 semi-liquid, mushy
	9	12	6	96.8	97.4	.....	....	2 semi-liquid, 1 liquid
	10	12	6	95.	97.6	.....	33	2 semi-liquid
	11	12	8	97.4	98.4	.....	34	1 semi-liquid, 1 normal
	12	12	9	96.4	96.2	.....	34½	2 normal
	13	12	9	96.2	95.6	.....	....	1 hard
	14	12	4	96.2	96.2	.....	....	4 semi-liquid, mushy
	15	12	2	96.	96.6	.....	....	5 semi-liquid, mushy
	16	11	14	95.2	96.6	Tea	....	5 semi-liquid
	17	11	10	96.4	97.4	B. M.	24	3 semi-liquid, 1 liquid
	18	11	11	97.2	97.8	.....	....	4 liquid with curds
	19	11	12	96.8	97.	3-6-1½	25 boiled	4 liquid with curds
	20	11	12	95.8	97.2	.....	....	3 semi-liquid with curds
	21	11	13	97.	98.	.....	....	3 semi-liquid
	22	11	13	98.	98.4	.....	....	2 semi-liquid
	23	12	3	98.	98.4	.....	....	2 semi-liquid
	24	12	9	98.4	98.6	.....	30 boiled	1 semi-liquid, 1 normal
	25	12	13	98.4	98.8	.....	....	2 normal
	26	12	14	98.6*	99	.....	....	2 hard
	27	12	15	....	....	.....	....	2 hard
	28	12	15	....	....	.....	....	2 hard
	29	13	4	....	....	.....	31 boiled	2 normal, 1 hard
	30	13	5	....	....	.....	....	3 normal
	31	13	5	....	....	.....	....	2 normal
Sept'ber	1	..	..	....	....	.....	....	2 normal
	2	13	6	....	....	.....	34½ past	1 hard
	3	..	..	....	....	.....	....	2 normal
	4	13	9	....	....	.....	....	3 normal
	5	..	..	....	....	.....	....	3 normal
	6	..	..	....	....	.....	....	2 normal
	7	13	10	....	....	.....	....	2 normal
	8	..	..	....	....	.....	....	1 hard, 1 normal
	9	..	..	....	....	.....	Fresh	3 normal
	10	13	12	....	....	.....	....	2 normal
	11	..	..	....	....	.....	36 fresh	2 normal
	12	13	14	....	....	.....	....	3 normal
	13	..	..	....	....	.....	....	2 normal
	14	14	..	....	....	.....	....	2 normal
				....	....	.....	....	3 normal

*Temperature normal thereafter. B. M. = Buttermilk.

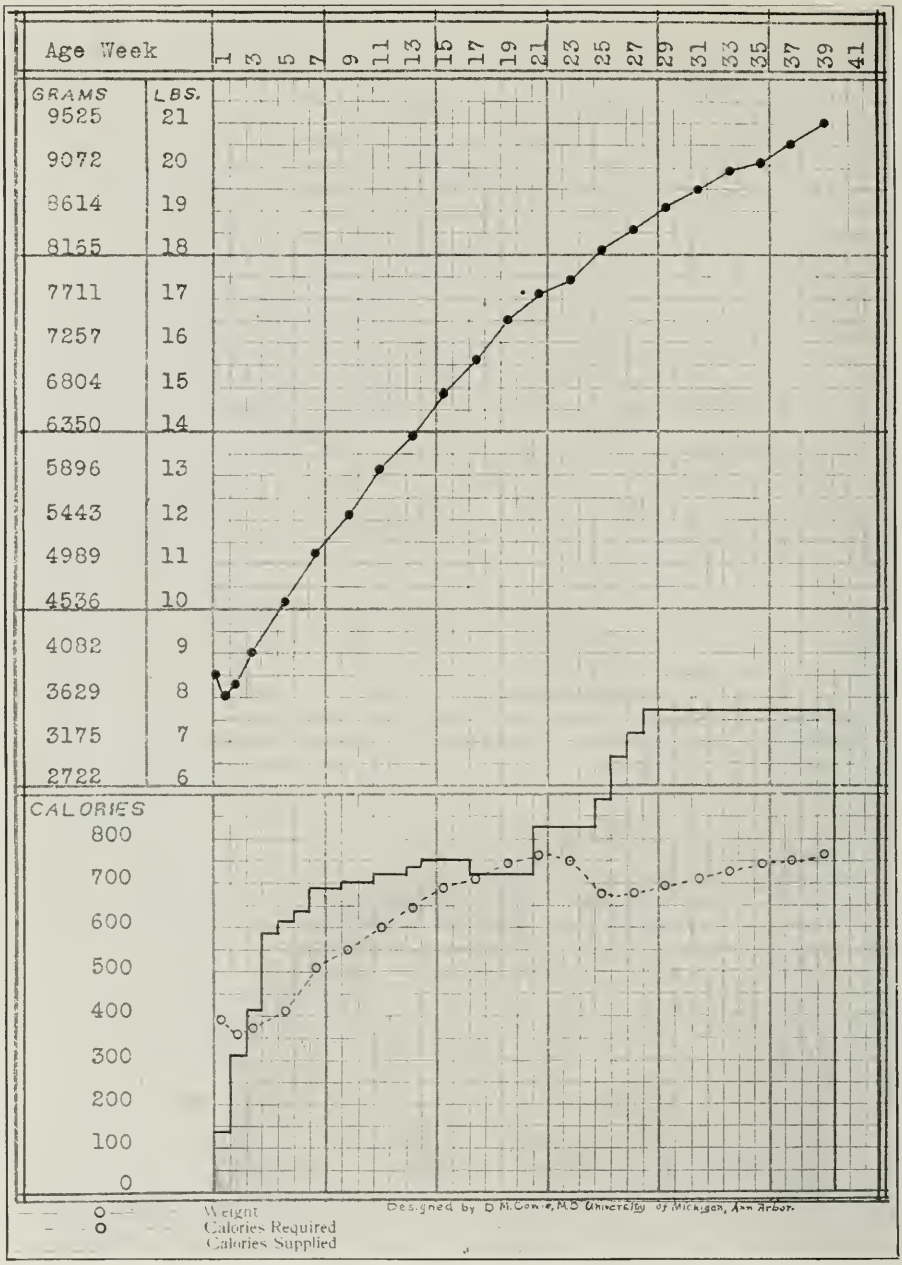


Chart 1.—This chart shows the average weight curve of a normal bottle fed infant, the energy line (calories of food required), and the amount of food (in calories) supplied by the maximum percentage formulæ quite generally employed by pediatricians in the United States. The chart further shows how correctly American children have been fed by the percentage method without reference to the "caloric method."

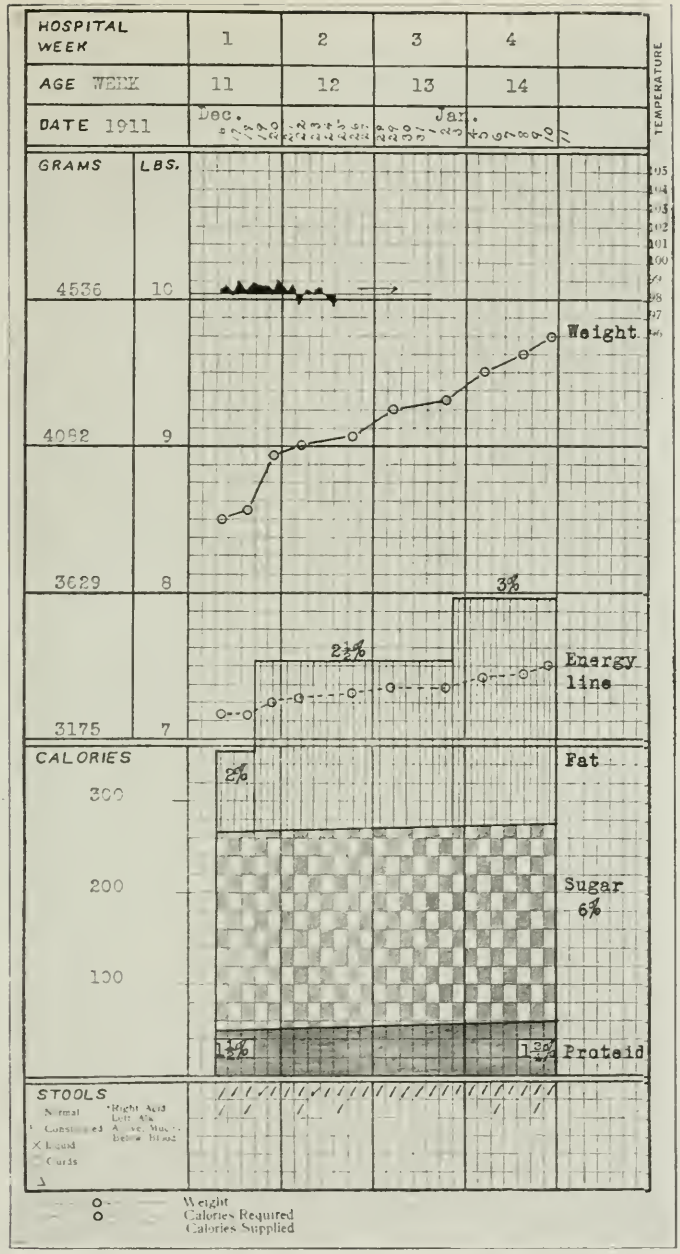


Chart 2.—Illustrating the minimum proteid requirement and the number of calories that must be furnished by sugar and fat to protect the proteid in its work of tissue building.

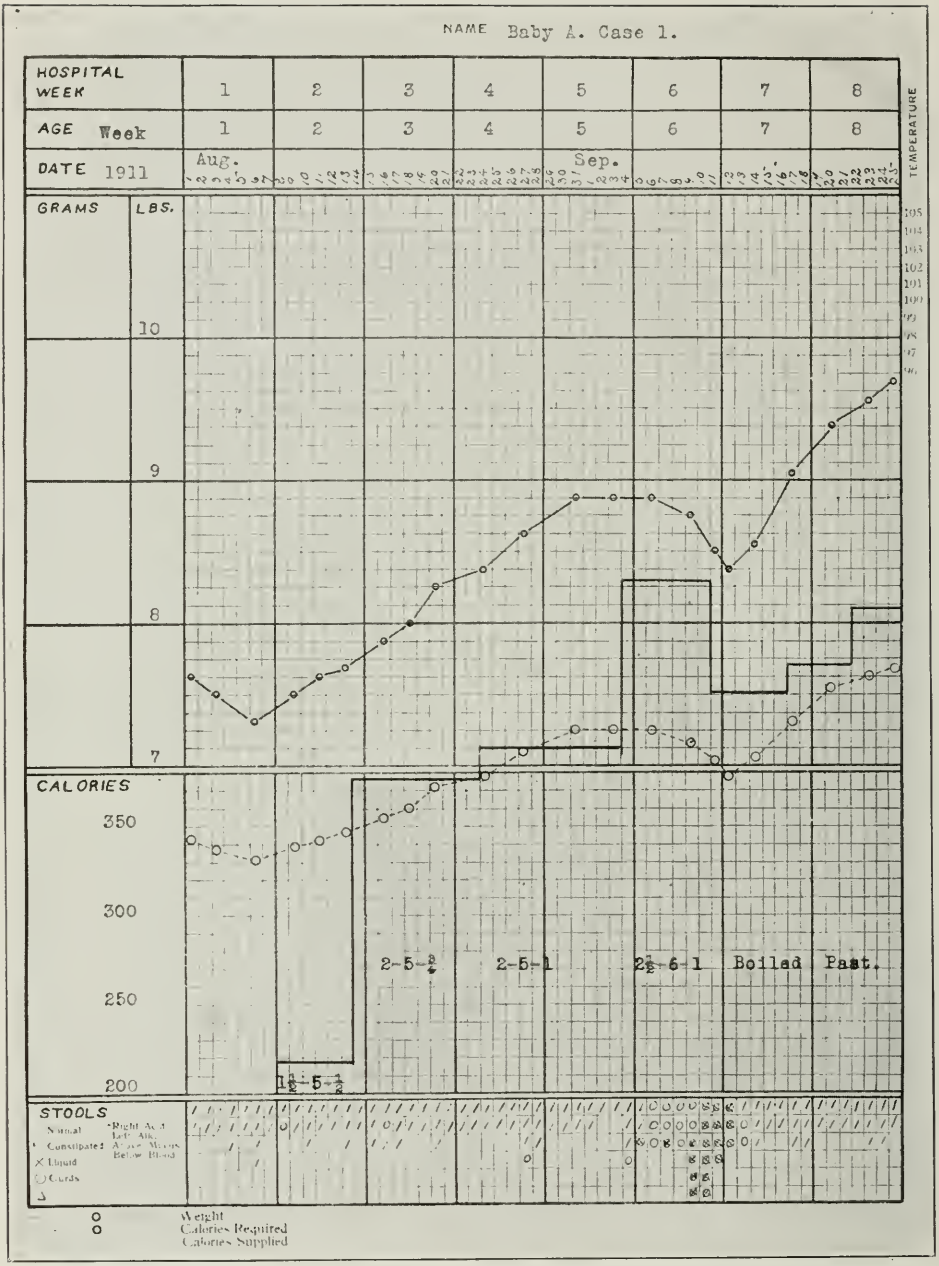


Chart 3.—1½-5-½ etc. = 1½ per cent. fat, 5 per cent. sugar, ½ per cent. proteid.

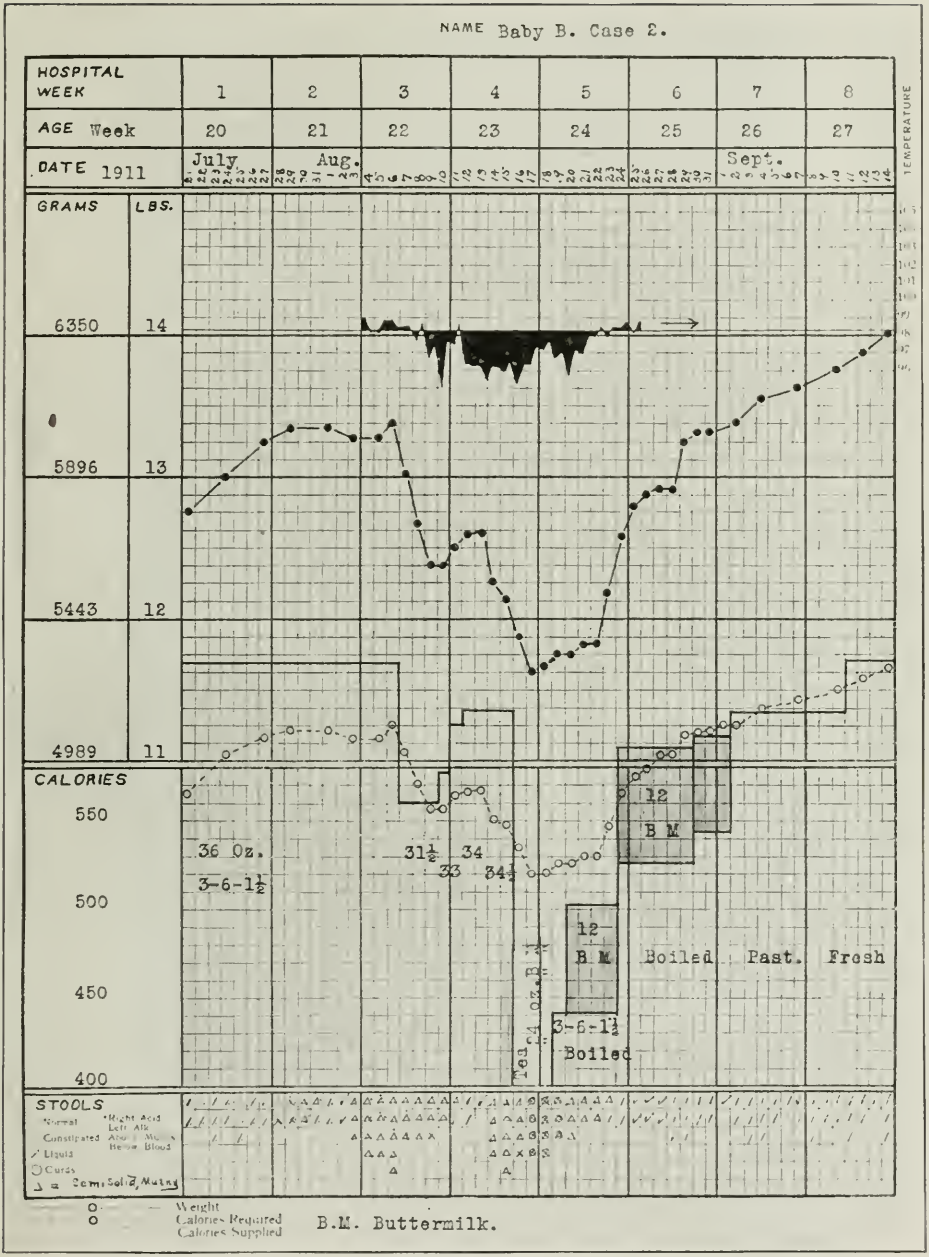

NAME Baby B. Case 2.
HOSPITAL WEEK
1
2
3
4
5
6
7
8
AGE Week
20
21
22
23
24
25
26
27
DATE 1911
July
Aug.
Sept.
TEMPERATURE
GRAMS
LBS.
6350
14
5896
13
5443
12
4989
11
CALORIES
550
500
450
400
36 Oz.
3-6-1½
31½
34
33
34½
12
B M
12
B M
3-6-1½
Boiled
Fed 0.5 B.M.
Boiled
Past.
Fresh
STOOLS
Normal
Constipated
Liquid
Curds
Weight
Calories Required
Calories Supplied
B.M. Buttermilk.

Chart 4.

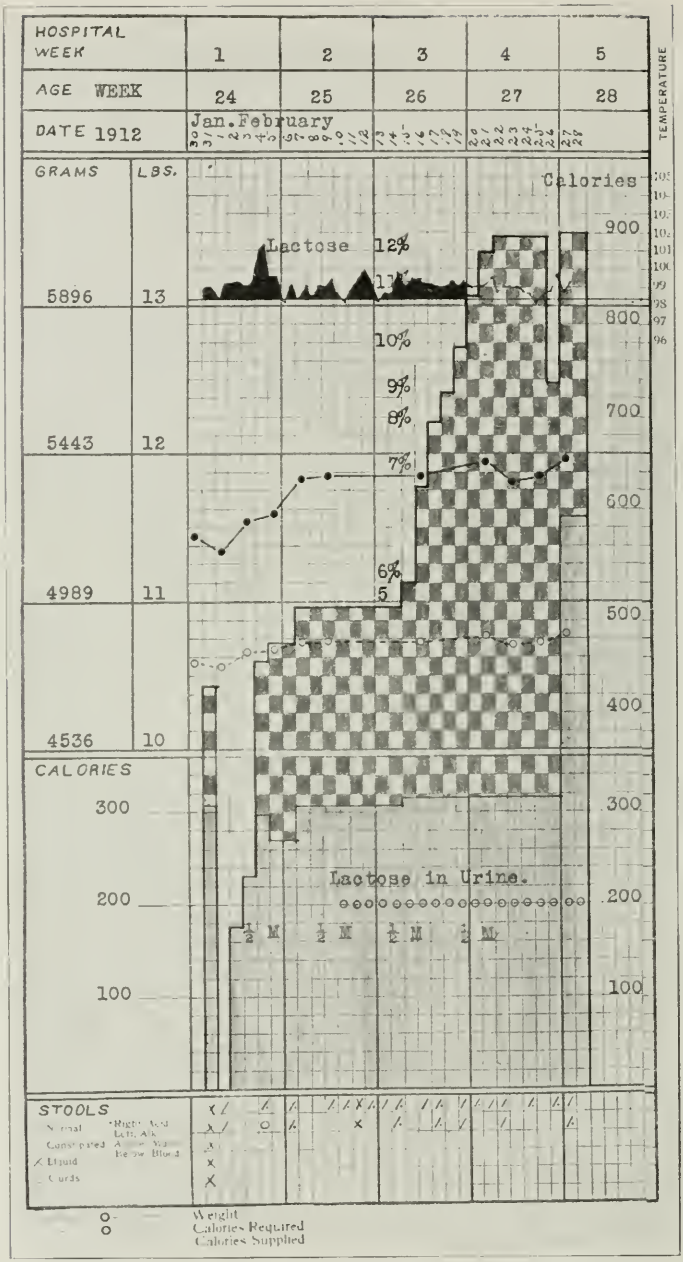


Chart 5.—Illustrating high sugar tolerance; ½ M = half milk. The checkered portion shows amount of lactose added to the ½ M.

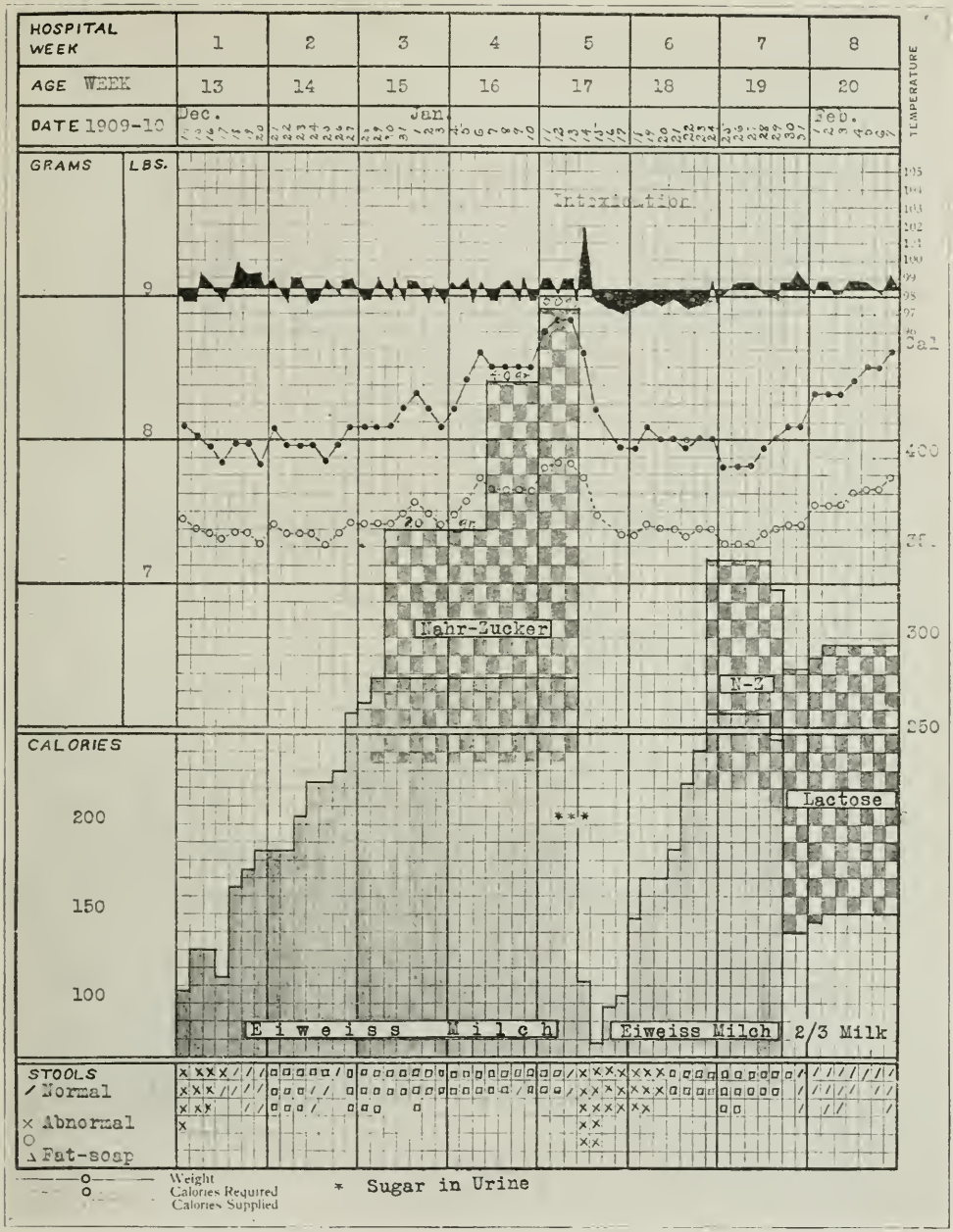


Chart 6.—Illustrating low sugar tolerance and resulting slight intoxication. The checkered portion below the *Eiweissmilch* line gives the approximate amount of sugar supplied in this food, above the line the amount of sugar added. The caloric value of the *Eiweissmilch* was doubtless higher than here estimated. Adopted from Finkelstein and Meyer. See text.

become acquainted with this basic or minimum protein requirement. He is now taught how to put this into practice by means of the chart. Chart 2 illustrates a simple case. By use of the accompanying table (2) he determines the number of grams of protein required and from this it

Chart 7.—Temperature, pulse and respiration curves in the case of Isabel K., a girl-baby, 10 weeks old, with normal digestion and normal stools. December 15 points marked xx 50 grams of 1 per cent. NaCl solution were given by gavage, December 16 at point x 100 grams of a 4 per cent. NaCl solution were given by gavage. There was no pyrogenic reaction following 1 gram of NaCl, but distinct reaction following 4 grams. There was also a marked respiratory increase and a pulse reaction. The stools increased in number and character after the ingestion of the salt solution.

becomes a simple matter to determine the percentage. He then chooses 5 or 6 per cent. sugar as a constant and makes up the balance of his calories from fat. In the present case the infant has been started on a

2-6-1.5 mixture. The protein has been gradually increased to 1.75 per cent. or 2 per cent. and the fat by steps from 2 to 3 per cent. As the protein is the tissue builder it is placed as the foundation stone in the food block. The daily quantity of food is readily determined as follows: In the present case, one ounce of 2-6-1.5 mixture has a caloric value of 14.8; 385 calories are required to bring the food up to the energy line. This number divided by 14.8 gives approximately 26 ounces, as the total amount of food. The food for a new patient is usually started a little below the line and later is pushed, as a routine, 30 or 40 calories above the line, to the approximate point of optimum tolerance.

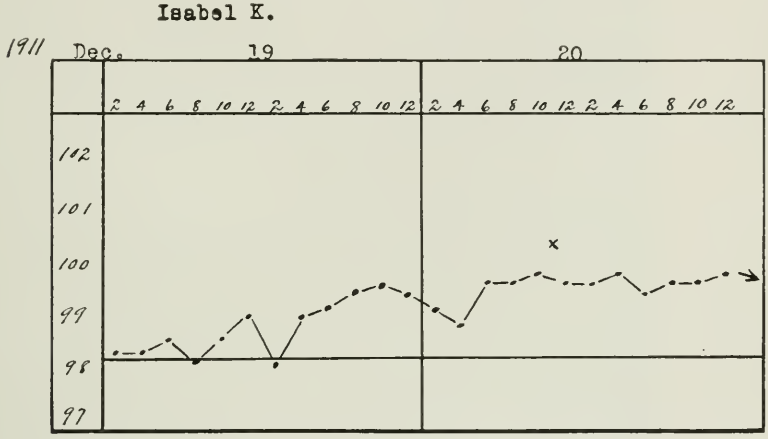


Chart 8.—Temperature curve in case of Isabel K. At point marked x 100 c.c. of 4 per cent. sodium bicarbonate solution were given by gavage. No pyrogenic reaction followed. The elevation of temperature was due to developing chicken-pox.

The student is now given a number of exercises to work out in order to familiarize himself with the keeping of a chart. He is furnished with blank charts, pencils, etc., and an instructor to explain all the steps taken. He first plots the weight-curve. From this he constructs his energy line. By the time he has figured this line for one chart it becomes an easy task for him to calculate caloric requirements. Next comes the plotting of the food blocks and the stools. The class is kept together on the first chart to avoid confusion. That is, all the members of the section start each division of the chart at the same time. The chart finished, the student discusses in writing the possible causes of the weight-drop and makes a

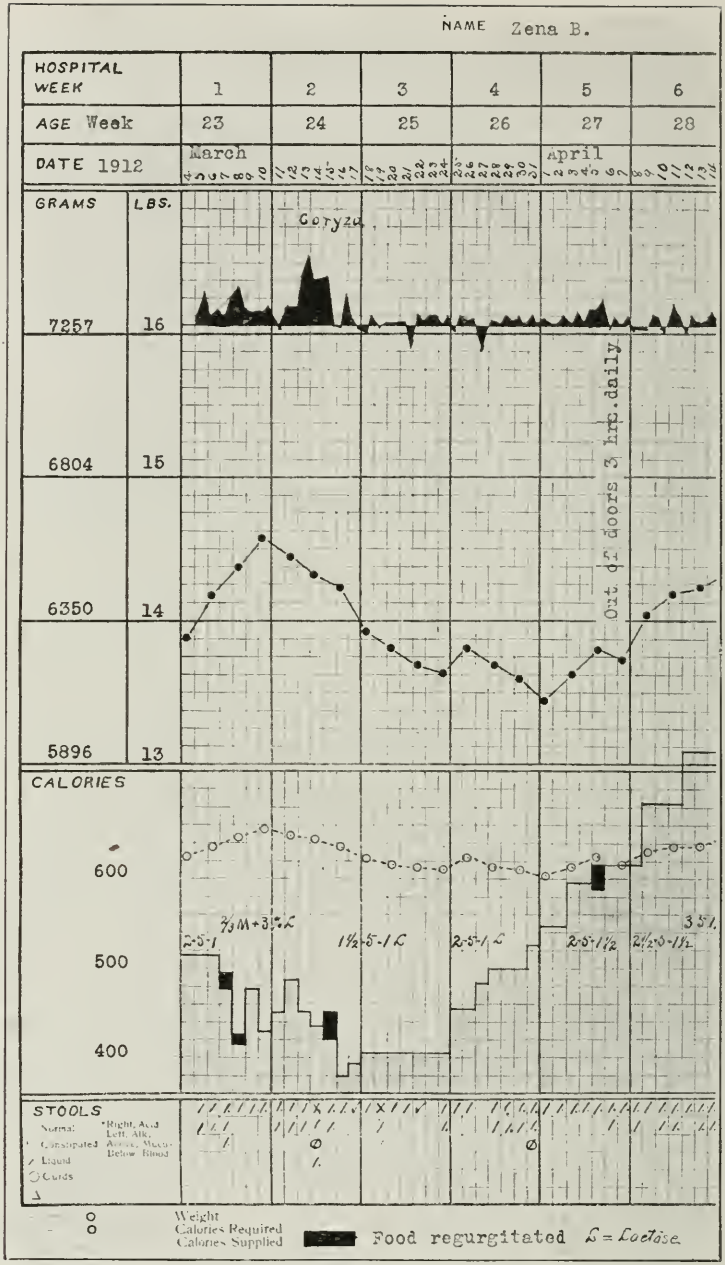
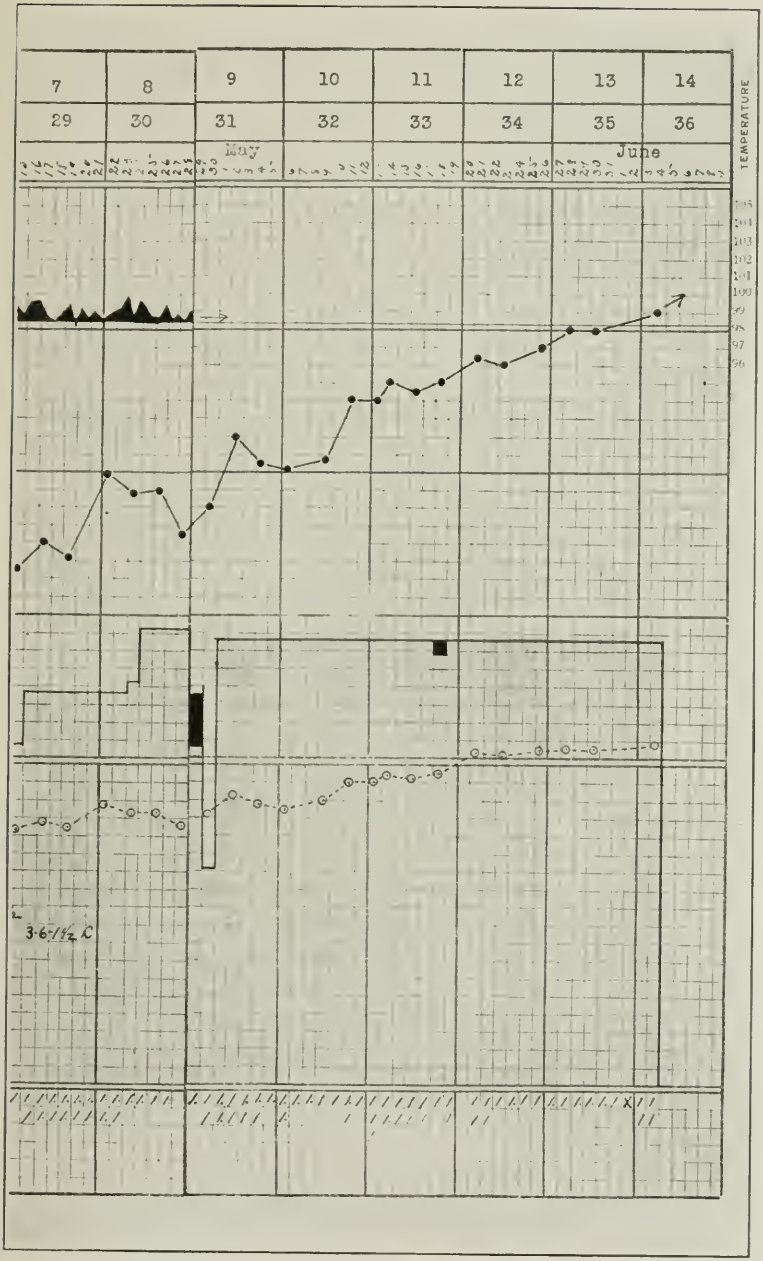


Chart 9.—A good illustration of the value of the energy lines (calories requir
dressings for club feet. In later weigh



ed). The gain during the first week is largely due to adjustment of plaster ings weight of dressings accounted for.

diagnosis. The completion of the chart takes almost invariably one and a half hours.

Chart 3 results from the first exercise and represents a case of simple dyspepsia from overfeeding.

Chart 4 results from the second exercise and represents a case of marasmus or the so-called decomposition. It has taken this infant eight weeks to gain 1 pound. This gain is accomplished by feeding close to the energy line. It illustrates low food tolerance. The primary drop in the third week is overcome by lowering the food below the energy line. A substantial gain is made with partial improvement in the stool, but when the food goes 50 calories above the line a relapse takes place. The further treatment of the case is self-explanatory. These two cases are almost entirely diagrammatic and are not given out as actual cases. Further exercises are given out to be done by the student at his home.

We next take up the study of sugar tolerance. This is illustrated by Chart 5, which represents an actual study of a case by the section.

In this chart a very marked sugar (lactose) tolerance is shown. In this normal infant on the seventeenth day, after a week of stationary weight, gradually increasing percentages of sugar were added, as indicated on the chart. When 5, 6, 7, 8, 9, 10, 11 and 12 per cent. are indicated, approximately 48, 53, 78, 90, 117, 126, 141 and 146 grams of lactose are supplied. While there was no increase in the weight, as might have been expected for a short time, there was no marked fall, no rise in temperature, no increase in the frequency of the stools and no sugar appeared in the urine. The rise in temperature during the first week was due to circumcision.

In Chart 6 just the opposite condition is recorded. On the addition of only 50 grams of sugar, or when the sugar in the food is approximately 7 per cent., distinct symptoms of intoxication are produced. Coincident with sharp rise in temperature there are a number of abnormal stools, a decided drop in weight and the occurrence of sugar in the urine. With a reduction in the food, particularly in the sugar content, the weight ceases to drop and does not rise again until the food block nears the energy line. In this case a substantial gain is recorded with the food 80 calories below the energy line.

I have constructed this chart (5) from one of Finkelstein and Meyer's cases.[1] The stools are supplied but they conform to the characteristics

1. Finkelstein and Meyer: Case 24, Curve 10, Jahrb. f. Kinderh., lxxi, series 3, xxi.

exhibited in mild cases of sugar intoxication and in infants fed on *Eiweissmilch*. In this case preceding the records here presented, during the twelfth week, while the infant was being fed buttermilk plus 5 per cent. lactose (making in all about 7.5 per cent. lactose) symptoms of dyspepsia developed with slight elevation of temperature. The improvement following the treatment with *Eiweissmilch* is indicated. There is first a period of seventeen days of practically stationary weight when with the addition of 20 grams Nährzucker, bringing the food line up to the energy line, the weight begins to increase until the point of intolerance is reached by the addition of 50 grams of sugar which brings the food 85 calories above the energy line. The characteristics of sugar intoxication and its treatment according to Finkelstein are indicated on the daily records which follow. With the exception of the weight-curve the chart bears little resemblance to the original from which the data was taken and converted into English terms.

This case brings up the subject of the effect of salts in infant feeding. During the period of buttermilk feeding in the case just mentioned there developed along with the dyspepsia a slight fever. It is not difficult to figure out the amount of salts the infant got during this time and one might reason that the dyspepsia and the intoxication following it some weeks later may have been due to injury of the intestinal epithelium by these salts. I therefore present some illustrations of the effect of feeding varying amounts of common salt to healthy babies. The following case will serve as an example. (Charts 7 and 8.)

Isabel K., girl baby 10 weeks old, with normal digestion and normal stools. On December 15 after a stationary temperature for eight hours and normal temperature prior to that time she is given by means of gavage in two doses an hour apart 100 grams of a 1 per cent. sodium chlorid solution, which represents 1 gram of salt. No pyrogenic reaction follows. Twenty-four hours later 100 grams of a 4 per cent. solution of sodium chlorid is given in one dose, by gavage. This represents 4 grams of salt. A distinct and marked pyrogenic reaction develops, reaching its height in six hours, declining to normal in eighteen to twenty hours. During the pyrogenic phase there is also a marked respiratory increase and pulse reaction as well as an increase in the number, and a change in the character of the stools. This phenomenon occurs with such great regularity when the proper amount of salt is given that it is very easy of demonstration before the class.

By Chart 8, and others which are not necessary to print, the specificity of the salts is illustrated. In this same case several days later the effect of sodium combination with the non-halogen element carbon is tried.

2. Dividing the dose as in the control makes no difference in the result.

Four grams of sodium bicarbonate produces no pyrogenic reaction and at this point it is shown that in milk the halogen combinations of sodium alone produce the pyrogenic reaction. It is therefore the sodium chlorid in the milk which is responsible for this reaction and is a constituent of the infant's food which should be considered in cases of obscure fever, diarrhea, etc., as well as the sugar and other constituents of the food. The subject of water retention by the sodium salts is also suggested at this time.

The student is now ready to go into the wards and follow his cases through. Since developing this chart method an interest in even the usually uninteresting cases has been awakened. The student feels that he is really doing something and although his visits night and morning to the ward are kept track of, the tendency to bolt has practically disappeared. I might record many charts like Chart 9, which have been kept by the students. This case shows the importance of carefully watching hospital cases. It is really difficult to do this without a graphic chart of some kind.

Zena B. (Chart 9), club foot, was referred to the pediatric department for nourishment. She was in one of the surgical wards in another building and away from the direct observation of the nurse in charge of the feeding cases. The intern had prescribed a 2-5-1 formula. The child made a good gain in its first week in hospital. On the fourth day the intern tried a simple milk dilution, bringing the sugar up to approximately 6 per cent. by an addition of 3 per cent. lactose. About this time the child developed a coryza with slightly abnormal stools, fever, and loss of weight. The fever subsided after four days, the stools became normal after one day but the weight continued to fall. On the twenty-first day the child was brought to the Palmer ward (Ped. Dept.) and a chart was started (Chart 9). It will be observed that the infant was being fed far below the energy line. The food was gradually increased to the energy line and pushed above it with the results seen in the chart. The black areas represent the number of calories lost through regurgitation. The marked regurgitation on April 29 following declining weight after marked increase in the food and refusing of the total quantity made us fear the development of a dyspepsia from over-feeding; consequently on the following day the child was fed below the energy line. No bad symptoms developing, the food was again pushed to just a little below the former point, with only one day of slight regurgitation in six weeks. The temperatures are all rectal. We find that a large per cent of our babies run a temperature like the one plotted, from the third hospital week on, without any discoverable cause. It may be well to state that the salt content in our percentage formulæ is never excessive. This chart is an exact copy of the one made by the student in charge of the case.

It is not the purpose of this paper to demonstrate any classification of the digestive disturbances of infancy. It is apparent how a chart can be

used to illustrate the various causes of stationary, declining and increasing weight with their attendant symptoms and signs.

The lessons we learn from practical use of a graphic chart are that changes in weight are usually explained at a glance; that a child cannot make substantial gain on feeding below its caloric needs; that he may often make a loss by feeding far above the line and that when strict attention is given to this point, with proper adjustment of percentages and attention to fundamental principles, most cases improve. There are instances in which the very best of care and thought cannot suffice to bring about improvement.

ACUTE YELLOW ATROPHY IN A CHILD THREE YEARS OF AGE

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Jaundice in the newborn, usually of a benign character, is of frequent occurrence. It may manifest itself in a yellowish tinge of the skin, which physiologically follows the hyperemia of the integument in the first few days after birth. Secondly, it may be due to the presence of bile pigment in the skin, due probably to changes in the hepatic circulation. It may be evident at birth; more commonly, however, it occurs two or three days later. The prognosis, as a rule, is good. In the so-called "icterus neonatorum," regarded as a physiologic rather than a pathologic condition, the urine and stools are not changed in character.

Much speculation regarding its origin has been indulged in and many theories now disproved or shown to be unreasonable have been promulgated. At the present time the condition is regarded as hepatogenous rather than as hematogenous in origin.

In a recent work from the Research Laboratory, Board of Health, New York City, Dr. A. F. Hess[1] presents a study of icterus neonatorum by means of the duodenal catheter. Some of the more prominent theories and recent views are given. As the result of carefully conducted experiments and findings, no new theory is advanced, but the following summary is presented: "Tests by means of the duodenal catheter show that bile is very rarely excreted during the first twelve hours of life; it was obtained but once in the course of fifty-two tests.

"Bile excretion during the subsequent twenty-four hours is variable; in cases of marked jaundice it is profuse; in cases not jaundiced it is scanty or absent.

"The function of excretion gradually becomes fully established during the first week or ten days of life.

"Where jaundice manifests itself, it precedes the excretion of bile into the duodenum.

1. Hess, A. F.: Am. Jour. Dis. Child., May, 1912.

"Secretion of bile varies within wide limits. In general, it is marked when the jaundice is marked.

"The occurrence of jaundice results from a defective correlation of excretion and secretion. It is generally caused by the inability of the rudimentary excretion to cope with the sudden profuse secretion of bile."

The article concludes as follows: "The reason why jaundice appears in the first days of life is because at the time when excretion has incompletely assumed its function throughout the body, in the liver as well as in other organs, for examples, in the breast and in the kidneys, a sudden flood of bile is poured into the passive excretory ducts and gains access to the hepatic circulation."

The mild type referred to above must be differentiated from the more serious conditions, the result of congenital syphilis, malformations of the biliary ducts or septic conditions originating in the umbilical stump.

In certain types of septic infections in the newborn, described as "Buhl's disease," extensive fatty degeneration of the parenchymatous organs is found post-mortem. Such cases must be regarded as unusually severe types of sepsis, in which particular symptoms are especially prominent.

In older children, if we except the cases due to alcohol and gall-bladder troubles, the same causes are effective as in adults. It is not our object to discuss fully cases of jaundice following duodenal catarrh with its various causes, the type due to emotional disturbances or the epidemic variety. Occasionally catarrhal jaundice is seen in infectious diseases, as pneumonia or typhoid fever. Osler says the nature of acute catarrhal jaundice is unknown. It may probably be an acute infection. Anomalous cases are, now and then, encountered.

Among the rare instances are the cases "met with in various conditions of unknown, but more or less obscure infective nature, variously designated as epidemic, infective, febrile, malignant jaundice, icterus gravis, Weil's disease, acute yellow atrophy." (Osler.)

There are all grades of transition between the simple catarrhal jaundice and the grave, destructive icterus, so-called acute yellow atrophy.

Acute yellow atrophy, as defined by Osler, is understood to represent jaundice associated with marked catarrhal symptoms and characterized anatomically by extensive necrosis of the liver cells, with reduction in the volume of the organ.

A. O. J. Kelly says: "Acute yellow atrophy of the liver is an acute and widespread autolytic necrosis of the liver cells characterized clinically

by jaundice, reduction in size of the liver, and toxic disturbances of cerebration, proceeding to a fatal issue."

In text-books it is stated that simple catarrhal jaundice lacks the features of general infection. Weil's disease, on the other hand, is a type of infectious jaundice in which fever, enlargement of the liver and spleen, nephritis and muscular pain accompany the icterus. These cases are usually of a benign character terminating in recovery. "From icterus gravis and acute yellow atrophy only the course of the disease and the absence of destruction of the liver cells can fully differentiate these benign cases; there is, in fact, a gradual merging of the types and no distinct border line."

In hypertrophic cirrhosis the symptoms of a profound icterus gravis may develop, with all the clinical features of acute yellow atrophy, including the presence of leucin and tyrosin in the urine, and convulsions (Osler, fourth edition, p. 551).

In cases of hypertrophic cirrhosis, which eventually end in atrophy, we should not be surprised to see acute yellow atrophy supervene, but that the latter should develop in the florid period of hypertrophy seems almost a physical impossibility. In a recent article, Auerbach[2] describes a case readily diagnosticated during life.

Acute yellow atrophy is rare. The best recent study of the subject is by F. W. White.[3]

J. Phillips[4] reports a case with autopsy in a child 5 years of age.

Rolleston has collected 22 cases occurring within the first ten years of life. One of our members, Dr. A. H. Wentworth,[5] reported a case in a child of 5 years. The cause of the disease is unknown; cases have been observed after various acute infectious diseases and in syphilis. It has followed acute alcohol poisoning, the ingestion of mushrooms and sausages, prolonged chloroform narcosis and phosphorus poisoning. It has occurred in livers of a normal type or when affected by chronic processes, such as cirrhosis or passive congestion, chlolangitis.

A study of the literature and pathologic conditions and findings leads inevitably to the conclusion that the designation of acute yellow atrophy, as well as icterus gravis, comprises a series of diverse disorders that exhibit more or less superficial resemblance. Cases due to syphilis,

2. Auerbach: München. med. Wchnschr., Dec. 26, 1911.
3. White, F. W.: Boston Med. and Surg. Jour., 1908, clviii, 729.
4. Phillips, J.: Jour. Am. Med. Ass'n., February 24, 1912, p. 586.
5. Wentworth, A. H.: Tr. Am. Pediat. Soc., xvii, 140.

septicopyemia, puerperal eclampsia, phosphorus poisoning, delayed chloroform poisoning, etc., can be separated from the main group, but the definite etiologic factor of a large proportion still remains to be determined.

It is greatly to be regretted that the history of the case reported below is imperfect. Unfortunately no data were obtained in a second case, in a girl 16 months of age, admitted to my service at Gouverneur Hospital October 2, 1910. This child was brought in on the ambulance in profound coma, intensely jaundiced and died a few hours later. Only a portion of the liver was obtained postmortem. Dr. B. Schwartz (associate pathologist) reported changes similar to those found in acute yellow atrophy.

Gussie K., 3 years of age, admitted to Beth-Israel Hospital (children's ward) November 26, 12 m.; died November 26, 10.50 p. m.

Present History.—Began gradually two weeks ago with slight jaundice, restlessness, white stools and apathy. Has had a low grade temperature for the last few days.

On day before admission it was noticed that the child could not see. A few hours later projectile vomiting set in and child became stuporous; twitchings of left hand were noticed. Child was brought to hospital in coma.

Physical general condition very poor, complete coma, respirations irregular.

Skin deeply jaundiced.

Eyes.—Pupils irregular, sclera jaundiced.

Heart.—Sinus irregularity.

Liver.—Dullness 1 inch below the free border of the rib (four fingers below free border four days ago).

Extremities.—Knee-jerks exaggerated.

Clinical.—Lumbar puncture: 25 c.c. clear fluid under pressure withdrawn. No albumin present.

Urine shows large amount of albumin, no casts. Bile present.

Blood.—White blood corpuscles, 19,000—70 per cent. polynuclears.

Temperature.—97-98 F.: pulse, 88-104; respiration, 30.

The profound coma, intense jaundice and rapid reduction in the size of the liver led to a probable diagnosis of acute liver atrophy.

Sincere thanks are herewith tendered to our pathologist, Dr. Eli Moschcowitz, for the postmortem and pathologic report.

Partial autopsy only permitted. Lungs and heart not removed.

Liver.—Enlarged, yellowish-red in color, surface smooth, edges sharp. On section firm, surface smooth; color pale red with greenish tinge. Surface presents a "marmorites" appearance, each lobule being surrounded by a yellowish narrow zone.

Gall-bladder normal in size, filled with green fluid bile. Ducts free.

Stomach normal.

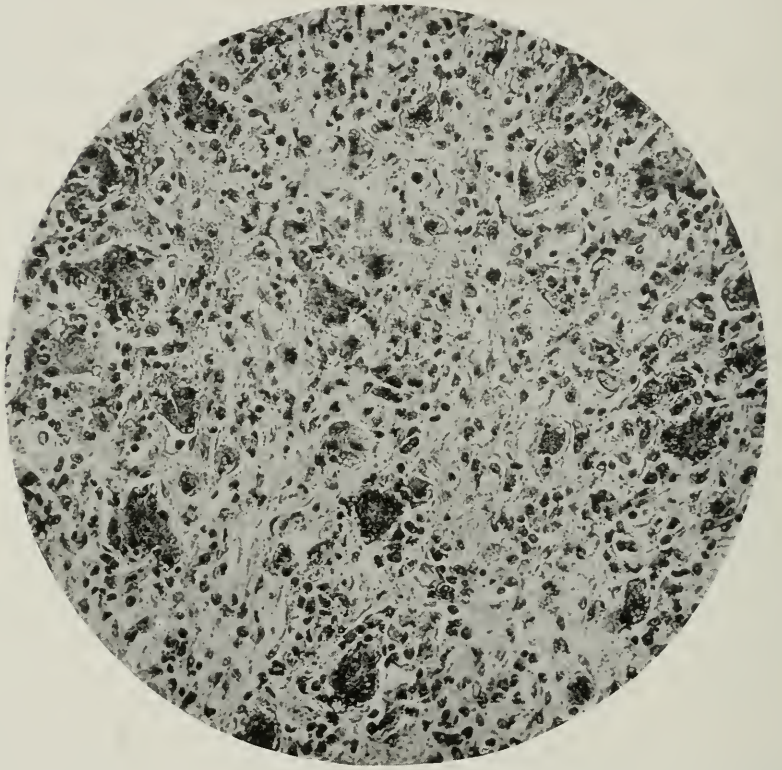
Spleen 6x3x1½ inches. Surface smooth. On section, firm, reddish-brown in color, malpighian bodies enlarged and prominent.

Kidneys enlarged, surface smooth, capsule strips easily. On section, light red in color, cortex thinned, markings cloudy. Bases of papillae slightly congested. Pelvis free.

Pancreas.—Firm, yellowish-gray in color. On section smooth, lobules in places indistinctly outlined; in these areas the organ is a trifle softer than normally.

Intestines.—Peyer's patches very prominent, otherwise normal.

Mesenteric glands much enlarged; smooth, firm, greyish in color.



Cross section of liver (magnified x 170), showing complete loss of normal histological arrangement, and extensive formation of new connective tissue. A number of deformed liver lobules are seen, the cells of which show some parenchymatous and marked fatty degeneration. A few isolated liver cells are also interspersed in the connective tissue. The connective tissue is infiltrated with round cells and a few polymorphonuclear leukocytes.

Anatomic Diagnosis.—Icterus, acute congestion and fatty degeneration of liver. Splenic hyperplasia; acute parenchymatous degeneration of the kidneys. Status lymphaticus.

Microscopic Report.—Liver.—The entire histologic arrangement of the liver is absent. Instead, we find a diffuse replacement of the liver structure with fibrous tissue in which the remains of the liver trabeculae are imbedded. The majority of these trabeculae have retained their original conformation, while others are merely represented by irregularly arranged groups of cells Isolated epithelial cells or groups of two or three are common. The majority of the liver cells stain well, others stain poorly, the nuclei being faint and poor in chromatin. The cell bodies are granular and merely contain fatty globules. In many cells the fat globules entirely replace the protoplasm. Histologically, the relation of the degenerative processes to the liver lobule cannot be determined with any accuracy, but it appears as though the peripheral portions of the lobules in the neighborhood of Glisson's capsule and the sublobular veins show a greater preservation of the liver trabeculae than the central portions. The connective tissue consists of fine fibrilla in which the numerous red blood-cells, round cells and cells resembling plasma cells, are abundant. Collections of round cells are common and usually occur near the capsules of Glisson.

The capsules of Glisson are well preserved and are infiltrated with a moderate number of round cells. The vein and artery show nothing abnormal. The bile ducts are well preserved and are empty. Newly formed bile ducts are numerous, especially in or near the capsules of Glisson. The central veins are nearly all obliterated. There is a diffuse biliary pigmentation in the connective tissue and in the remains of the liver trabeculae.

Spleen.—The malpighian bodies are very large and have a large chyme centrum. The splenic veins are enormously dilated and the lining endothelium is much swollen. The trabeculae are not increased in number or size.

Kidneys.—The cells of the convoluted tubules are swollen, poorly demarcated and coarsely granular in appearance. The nuclei stain faintly. The lumina contain a moderate amount of cellular and granular débris. The glomeruli are congested and do not entirely fill the capsule; the resulting spaces contain small amounts of granular material. There is moderate congestion, especially in the cortex. Papillae and pelvis normal.

Pancreas.—Considerable area of autodigestion, otherwise normal.

Intestine and *stomach* normal.

Mesenteric Glands.—Diffuse hyperplasia.

DIAGNOSIS OF ACUTE YELLOW ATROPHY

In the early stage, there are no characteristic symptoms to arouse suspicions that we are dealing with more than an ordinary catarrhal jaundice. The development of nervous symptoms should put us on our guard and lead to a more careful examination of the urine for the presence of leucin and tyrosin. As the case develops the jaundice becomes more pronounced; vomiting persists, with possibly hematemesis or the appearance of purpura. Headache, noisy delirium, restless, followed by coma and possibly convulsions, quickly lead to a fatal termination. In the early stage the liver is slightly enlarged and tender. Death may occur before the liver diminishes in size.

Lindsay S. Milne[6] says: "Acute yellow atrophy, as is well known, is an extremely widespread rapid necrosis of the liver. The term atrophy is therefore a misnomer."

He believes it to be more common than usually so considered, for in the past its conception has been based on an altogether too classic picture from the clinical and pathologic view. There is a wide latitude in its duration, clinical type and pathologic appearance depending on the degree of hepatic destruction.

Milne further states, in children in particular, a protracted course is the rule. In the article referred to above, subacute liver atrophy is fully discussed. An additional case with complete pathologic findings is reported.

Ten cases have been reported by this author of which number five have been reported.[7]

"Subacute atrophy, like acute yellow atrophy, is not a real atrophy, but the result of a necrosis and the subsequent inflammatory repair. As in the acute cases, the necrosis is more or less rapidly accomplished, and the longer duration of life in the subacute, or recovery in the chronic cases, depends largely on the amount of liver destruction and its recuperative power."

From his careful studies Milne adds: "In conclusion, one can trace a direct connection acute yellow atrophy, subacute atrophy and cirrhosis of the liver in all its types, the difference in each depending on the extent and rapidity of accomplishment of the destruction of the liver."

6. Milne, Lindsay S.: Arch. Int. Med., Nov. 15, 1911.
7. Milne, L. S.: Jour. Pathol. and Bacteriol., Cambridge, 1909, xiii, 161.

INFANTILE SCURVY AND MODERN CONDITIONS

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"I had clean forgot scurvy." So said a doctor after treating "rheumatism of the legs" for two weeks. He was a good general practitioner of long experience. He said that though he had known scurvy, it had been so long since he had seen a case that the old traditions of rheumatism had quite blotted out the later impression of scurvy.

Here is the reason for the existence of this paper. There once was a time when there was no scurvy, as there was no gold in California till '49. Then there followed a "fever" of interest and everybody was hunting for this new disease, finding even slight and beginning cases. Upon this ensued a period when scurvy was anticipated by prophylactic orange juice and but little scurvy developed.

The case referred to above came into the Presbyterian Hospital last September and on entrance showed the paralysis and attitudes represented in the photographs of Series One. To this audience the diagnosis is as clear as the moon in the sky, and when I add that the child had spongy gums and a "black eye" it will seem that the old practitioner and the very new beginner need a reminder. Boiling milk an hour is no longer in vogue, condensed milk is not popular, but malt soup is. The proprietary foods are still selling and a new generation of young graduates is overflowing the land and they know not the traditions of the fathers. If I mistake not we have new conditions to meet. To safeguard milk it is to be pasteurized, to make sure it will "keep" there may be a tendency to carry the process rather far. In addition to that there are good chances that the family may yet boil it good and hard at home.

The mother nursed the child here pictured three months at the breast. For some reason she then weaned it. Seven consecutive months thereafter she fed it on Loefflund's malt soup. The doctor was German and this was a favorite food with him. It is used by most baby-feeders, but seldom, however, for so long a time as seven months without interruption. I may add that the same fault appears to be active in most cases of

scurvy, viz., a good food has been ridden to death (to mix the metaphor and forget to mix the food). Without describing the method of making this food (malt soup), it is well to recall that all the ingredients have been boiled. Whatever the essential cause of scurvy, long continued feeding on a food which is monotonously the same and at the same time insufficient, is a promient factor in the etiology of the disease. "Persistent deprivation of fresh food" is a frequent expression in the literature.

The doctor sent the case to my service in the Presbyterian Hospital, stating the diagnosis to be rheumatism and that he had tried a list of remedies which, though they revealed a great and intimate knowledge

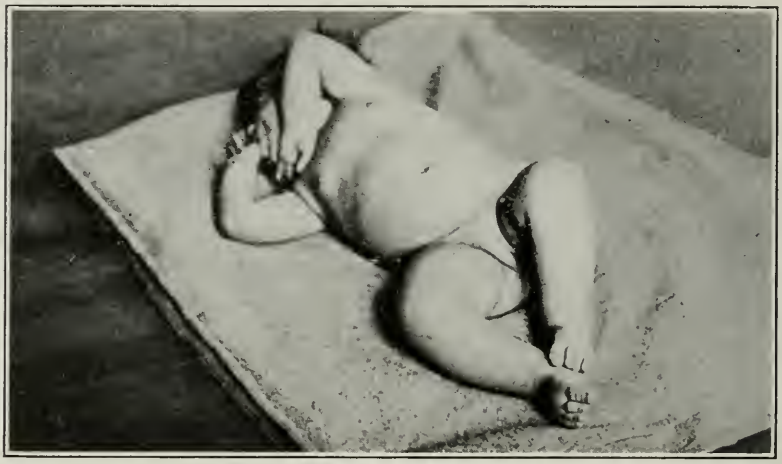


Fig. 1.—Showing pseudoparalysis of right leg, and attitude of restraining motion on admission.

of chemicals and drugs, did not say a word about fruit acids. The case entered by way of the accident ward and seemed to interest the two members of the house staff, who bent their noble brows low in thought for some time, just long enough, in fact, to allow my section class to get out of the building and so escape seeing a typical case of a disease not now very common in these parts. It may appear that errors of diagnosis are still possible, largely because the disease is so seldom seen that one cannot remember the diagnostic points. Hence this paper.

The first illustrations show the condition of the legs on entrance; the second series after two weeks of corrected regimen and treatment

with fruit juice; again another series, the last, after one month, showing complete recovery.

On entrance the symptoms were paralysis of one leg with diffuse swelling of the right leg rather more than the left. On the inner aspect

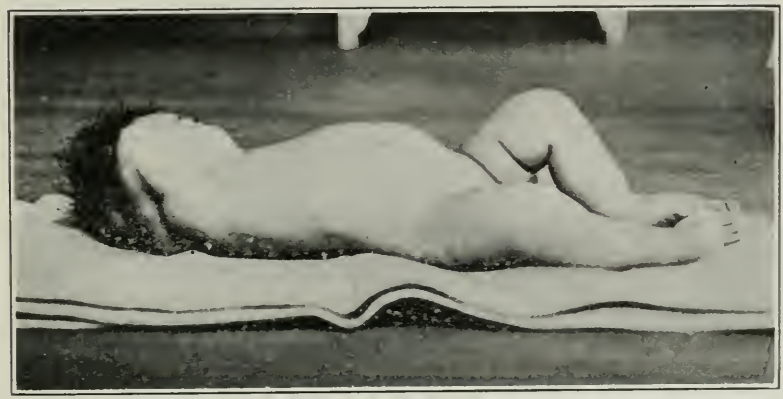


Fig. 2.—Same child as Fig. 1—different position.

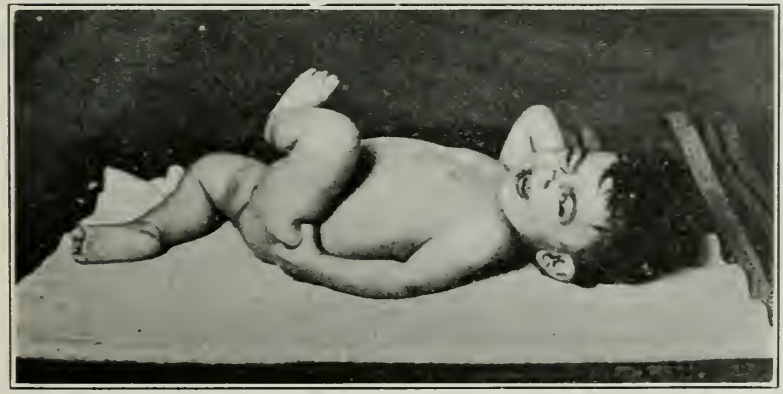


Fig. 3.—Same child after two weeks' treatment. Left leg freely movable.

of the right ankle there was a diffuse black and blue spot. The legs were flexed and immovable, exquisitely sensitive to the touch, to say nothing of moving. The patient could not move even the toes of the right foot. Arms were freely movable, not painful. The next notable

feature were the spongy gums. About the three teeth on the upper row and about one incisor on the lower there was swelling with congestion. It should be said that the teeth of the upper row were not quite through, but almost. Spongy gums are observed only where the teeth have cut

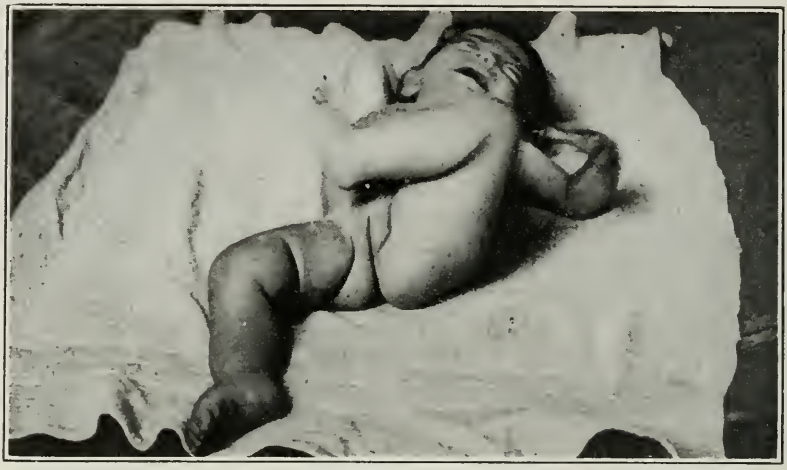


Fig. 4.—Same after two weeks' treatment. Right leg still weak.

Fig. 5.—Complete recovery after four weeks of treatment.

through or are just beneath the mucous membrane. The last of the three prominent features of this diagnosis was slight hemorrhage into the upper eyelid, a "black eye" on the left side, later to be followed by a

similar condition on the other side. The second eye was foretold and it seemed to the staff interesting that it came as predicted and resembled the other.

Treatment.—First, correcting the regimen, changing from all boiled or cooked food to fresh milk. To be strictly correct, the milk was not heated at all until the time of feeding. It was diluted with barley water, that is, "modified."

Second, the child was given orange juice twice a day, each day giving it a little more than on the previous day.

Results of Treatment.—It is not necessary to say much about this to one who has seen a case progress toward cure. To one who has not, I

Fig. 6.—Same, showing very free motion of both legs.

may say, as I say each year to students, "There are three miracles which a doctor can perform—one is by intubation to relieve croup, one the improvement of cretinism by the use of thyroid extract, the other the cure of scurvy by fruit juices. I consider my contention maintained in the case of scurvy.

In three to five days the pain in the legs began to subside, in two weeks the child was gaily waving one leg, and at the end of the month it was free of all pain, waving both legs equally. It allowed any amount of handling and was discharged from hospital without a vestige of anything by which one could have a suspicion of the disease because of which it had been admitted to the hospital. The miracle was performed.

Scurvy was first noted as a disease which might be a part of children's repertory, when Cheadle and Barlow obtained autopsies on a few children dying of what was sometimes called acute rickets. This term did not satisfy the lesions that began to attract the attention of hospital observers. This was coincident in time with the appearance, in England, of proprietary foods.

In May, 1889, I made an autopsy at the Foundling Asylum on a child which was thought to have died with acute hemorrhagic syphilitic periostitis, and I so reported it to the New York Pathological Society. It nearly passed as a freak case of syphilis, a curiosity only to be found in a vast metropolitan asylum. One member present, Dr. Van Santvoord, said the case reminded him of one occurring in his experience on Ran-

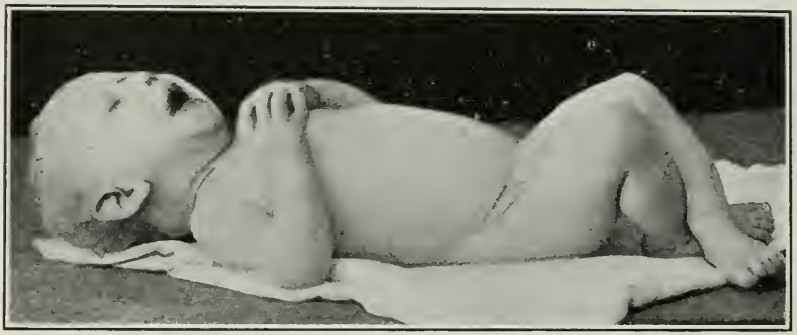


Fig. 7.—Characteristic attitude in scurvy. Immobile legs and arms and signs of discomfort.

dall's Island. His case was a helpless idiot, 6 years old, which died of hemorrhage about the femora and separation of the epiphyses. He had not recorded the case, and, in fact, had not fully understood it at the time, but subsequent reading had convinced him that it was a case of scurvy.

At the May meeting of the Pathological Society was recorded the first case of scurvy recorded from American practice. The autopsy of this case is referred to above, autopsy and record made by myself.

Keating's Cyclopedia, then on the market, contained an article on "Infantile Scurvy," written by an Englishman from English practice. Just at this point I was called to a real, live case, exemplifying in most striking dramatic manner the marked characteristic attitudes and hemor-

rhages of well-developed scurvy. It recovered on orange juice, recommended by the English writer. With a complete autopsy and a brilliant recovery it is not to be wondered at that I was hot on the chase for more. I read the reports of these cases at one or two private medical societies and thus learned of more cases that lay far back in memories of some present. By September, 1891, at the meeting of the American Pediatric Society, I had unearthed eleven cases, which I there reported.

At this meeting (September, 1891) my paper was lying on a chair awaiting the time for its reading when Dr. Osler came in, picked it up, asking what I was about to read on—what subject. On reading the title he said: "'Eleven Cases of Scurvy'? My book has just gone to the printers and I could not find a single case of scurvy (American) recorded."

It may be of interest to this Society to recall that meeting. It was in September, 1891, Arlington Hotel, Washington, Dr. T. M. Rotch in the president's chair. The paper was discussed by Drs. Rotch, Holt, Jacobi, Putnam, J. Lewis Smith and Fruitnight. Among those present were Osler, O'Dwyer, Vaughan, Forchheimer, Busey and Adams. It was at this meeting that the American Pediatric Society was admitted to the Congress of American Physicians and Surgeons.

For a couple of years scurvy made no further history with us. No one looked for it. One saw it when one fell over it. Then the fever began and you recall the rest. Every one found scurvy, even before its full development. By prophylactic treatment it ceased to be frequent, and we arrive at the present when it is so uncommon or even rare that few students have the opportunity to see a case. We may now look for the pendulum to get so far over the line of repose as to let in more and more mistakes in diagnosis.

As I was swinging from a trolley strap to land at the hospital corner Dr. McCosh was about to get on board. "Oh, yes," said Andy, "tell me quick, What are the signs of scurvy?" Answer: "If the mother says rheumatism of the legs and you find spongy gums, that's scurvy." "Right," said Andy, and he caught his car.

With more time in which to answer that question I might have added to advantage, "spongy gums and further evidences of hemorrhage," and the ground for diagnosis could be easily memorized.

The purposes of this paper will be fulfilled if the general practitioner shall here find a little help to carry in memory the salient points of diagnosis to a nutritional disturbance which, unchecked, may lead to disastrous results and may lose him the joy of working a miracle.

Finally, scurvy in infants concerns us at present:

1. Because with the introduction of pasteurization the tendency will probably be to boil the milk to insure its keeping; in other words, the cupidity of dealers will have to be reckoned with. Cooked milk is conceded to produce conditions favorable to scurvy.

2. Because it concerns the practitioner. Bear in mind the present case—a practitioner treated it for rheumatism for weeks.

3. Because it concerns the surgeon. Among the eleven cases first reported there were a couple in which the general surgeon diagnosticated sarcoma of the bone, abscess beneath the periosteum, putting in a trochar and aspirating blood. You will recall that one thigh is usually more swollen than the other; it is hard, exquisitely tender, and the diagnosis of abscess not so strange.

4. Because it concerns the orthopedist, and him most of all. The paralysis is marked and the case finds its way to him most naturally. I am inclined to think he sees more than any other.

5. Because it concerns all medical specialties.

6. Because cases occur just seldom enough to allow everybody to forget. Then, too, new generations come along who have never fallen over this wheelbarrow and consequently are not familiar with the rough and tumble fall which a wheelbarrow can give.

FEEBLE-MINDED CHILDREN: WHAT SHALL WE DO ABOUT THEM?

CHARLES P. PUTNAM, M.D.
BOSTON

There is a branch of pediatrics to which the society has given very little attention. I mean the study of feeble-minded children.

We call children normal who can, at a reasonable age, understand what is said to them, who can think and express themselves, can make profitable use of the ordinary schools, and who give promise of being able at least to look out for themselves when they are grown up. But dwelling among and rubbing shoulders with these so-called normal children are found some that fall below this standard who will not be able to look out for themselves in after life, and who are incapable of some or all of the performances mentioned above.

Among these children the most important are not those of the low grade, the idiots and imbeciles (who are generally recognized as such, and kept more or less under care and treatment), but those of higher grade, the best of whom look at first sight like normal children. It has been estimated that there are two hundred thousand decidedly feeble-minded persons in the United States, and that of these probably only about nine thousand are in institutions. The true numbers are doubtless much larger. These children are a great burden to the community. In the family they monopolize time and trouble, to the detriment of the normal members; in the school they hold back the better pupils, while acquiring but little themselves.

They are often punished for errors which they have not mind enough to avoid; and they are not prevented by this disciplinary method, or by any other, from setting fires, and without truly realizing the nature and logical results of their acts.

They constitute a large percentage of every reform school for boys or girls, and of the prisons as well; and in all these institutions they interfere seriously with reformatory influence.

Unless carefully guarded at home, or placed in institutions, they become loafers and vagrants; and being sexually passionate the boys beget and the girls bear illegitimate children; or when later married, as

they often are, also legitimate children. Of these children a large proportion, whether legitimate or illegitimate, are themselves feeble-minded. They are frequently carriers of venereal disases.

To the graduates of most medical schools no teaching on this subject has been given. Most doctors, on finding a serious misfit in a family or school, must begin his studies on this important and to him new subject, and will have to go for this purpose to books written only exceptionally by physicians, but mostly by psychologists. The individual case is usually discovered by the social worker, and brought before the physician, who is generally at first incredulous, and he finds out only by degrees that he has seen many such without realizing it.

The subject is so new to every one that no adequate and satisfactory classification of the cases has been made; and even the best authorities are not prepared to say just what ought to be done with the great army of patients in order to protect them and society, and to bring about as soon as possible the suppression of the disease.

At present segregation and special education are the recognized methods, and the public is developing a lively interest in an anti-feeble-minded crusade; but among the crusaders, physicians, and especially pediatrists, are too seldom found. Yet certainly the latter are the very ones to appreciate peculiarities in the minds of children, from their familiarity with the development of the normal mind.

My hope is, therefore, that the American Pediatric Society will appoint a committee to consider the subject of feeble-minded children, and report at the meeting of 1913, with authority to send information from time to time, at its discretion, to members of this society, but to no others, and also to ask information from said members: also, that members of the society will do what they can to introduce the subject of feeble-mindedness as a part of the curriculum, and also to encourage the segregation and education of such children, to the end that they may no longer continue and increase.

PROBLEMS OF INFANT FEEDING ILLUSTRATED BY CASES AND CHARTS

PERCIVAL J. EATON, M.D.
PITTSBURGH, PA.

In presenting this series of cases we have in mind bringing to your attention certain facts, and perhaps some indications of their relations to certain theories which we consider fundamental in the artificial feeding of infants.

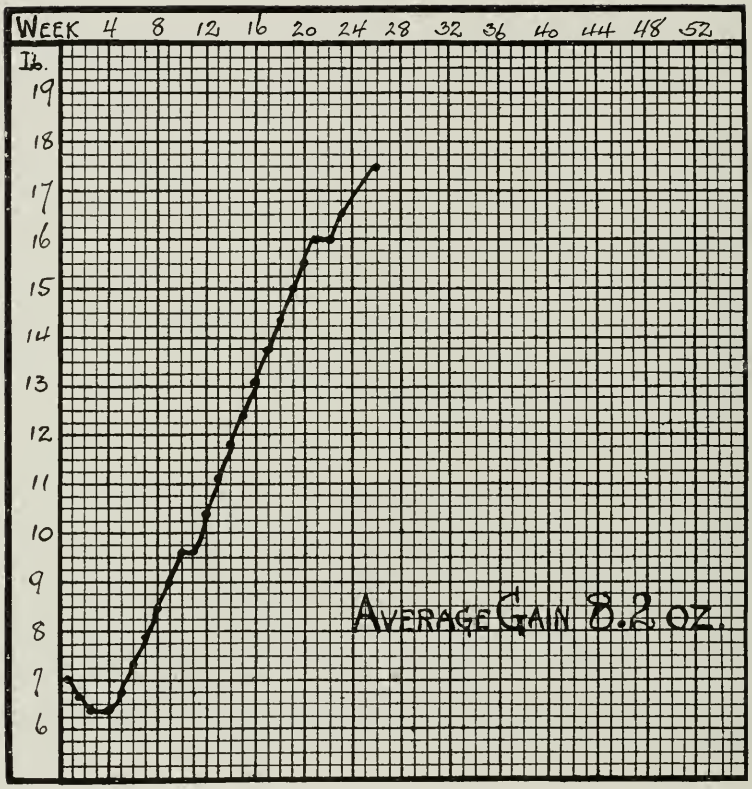
Certified milk was used in all cases where possible and gravity cream (averaging 16 per cent. butter fat). No mixtures were ever sterilized or pasteurized. All schedules and directions were written out, even to hours of feeding, and stress laid on the carrying out of all orders at the expressed and proper time. These cases could be multiplied many times, but we have selected those which were most available, and have given you some cases of rather slow gain, and some of rather extraordinary gain, the average lying somewhere between the two.

CASE 1.—Was brought to us during its fourth week, then weighing 6½ pounds. It had been irregularly fed by a very nervous mother, was hungry and had much colic. The child was put on a schedule of feeding hours and attempts were made to improve the breast milk. The baby was restless and hungry notwithstanding, so that during its fifth week it was given whey enough to assuage its hunger, and it gained a little. During its seventh week the breast milk decreased so rapidly in amount that the child was put upon a formula. The baby began to gain well, and soon, from the utter failure of the breast milk, was on modified milk. It has gained consistently, except during its eleventh and twenty-sixth week. During the eleventh week the mother was ill and a nurse cared for the baby, but was not regular and the baby fussed a great deal. During the twenty-sixth week the baby had a bad catarrhal cold. The formula was changed whenever the baby was not satisfied. It is well, flesh hard, color good, and it is very active.

No. 1.

Formula	1	2	3	4	5	6	7
Fat percentage	2.0	2.0	2.42	2.66	2.66	2.66	2.66
Proteid percentage	1.31	1.31	1.59	1.75	1.75	1.83	2.08
Amount in ounces	24	32	33	42	48	42	42

CASE 2.—Was seen first when eleven weeks old. Had not gained much for five weeks and was very restless, hungry and colicky. Attempts were made to increase the quantity and quality of the breast milk, but during its twelfth week, in addition to both breasts, was given an ounce or two of whey at each feeding.


WEEK 4 8 12 16 20 24 28 32 36 40 44 48 52
lb.
19
18
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15
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13
12
11
10
9
8
7
6
AVERAGE GAIN 8.2 OZ.

Figure 1.

The child began to gain, but the breast supply steadily diminished and modified milk has since been its food. Has gained consistently, is firm of flesh, has a fine color, is contented and happy.

No. 2.

Formula	1	2	3	4	5	6	7	8	9
Fat percentage..	2.3	2.3	2.4	2.3	2.51	2.37	2.37	2.56	2 56
Proteid percentage	1.37	1.50	1.57	1.71	1.65	1.69	1.81	1.87	2.+
Amount in ounces	28	35	40	49	51	54	54	56	56

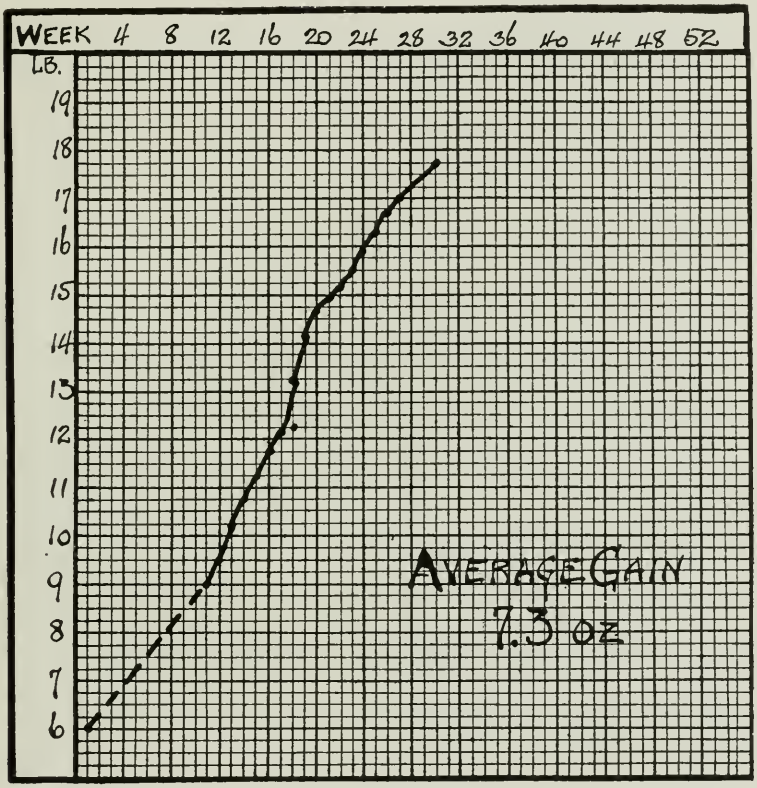
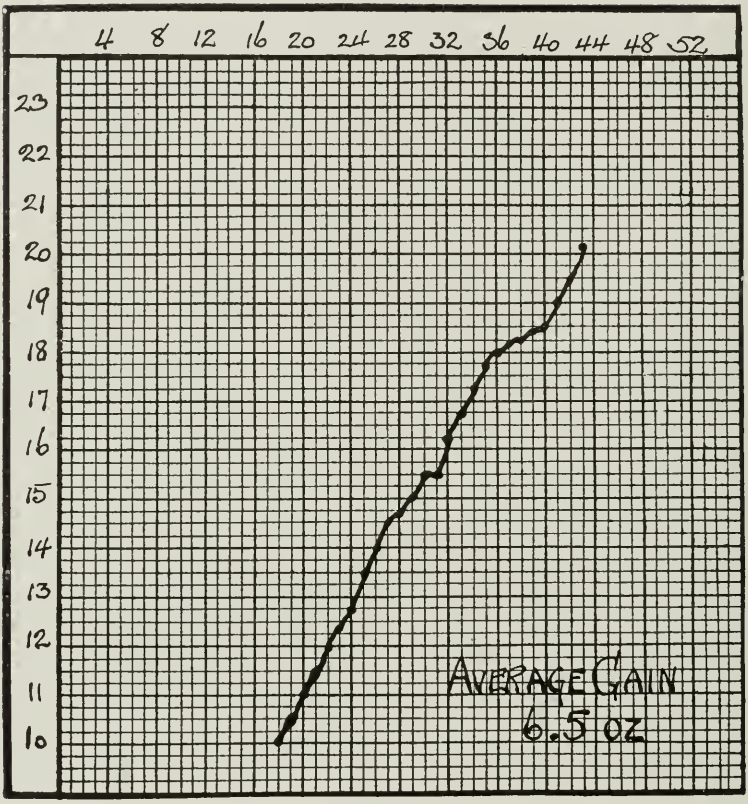


Figure 2.

CASE 3.—M. E. B., born July 20, 1911, initial weight 7½ pounds, was brought to us during her eighteenth week: then weighed just 10 pounds, was very pale and hungry. Mother had had some mastitis and was giving baby right breast only and a formula. Baby was constipated. The chart indicates the strength and the amount and also the gain. The last two or three weeks has not gained so much, but has been attempting to erupt teeth, and is not quite so happy.


4 8 12 16 20 24 28 32 36 40 44 48 52
23
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10
AVERAGE GAIN
6.5 OZ.

Figure 3.

No. 3.					
Formula	1	2	3	4	5
Fat percentage	2.66	2.66	2.66	2.66	2.66
Proteid percentage	1.40	1.55	1.75	1.83	2.—
Amount in ounces	30	36	42	42	48

CASE 4.—W. McC. M. At birth weighed 8 pounds, 14½ ounces. Mother nursed it for a little more than three weeks, but during that time it had to have whey to satisfy it. About that time the mother had an attack of ptomain poisoning

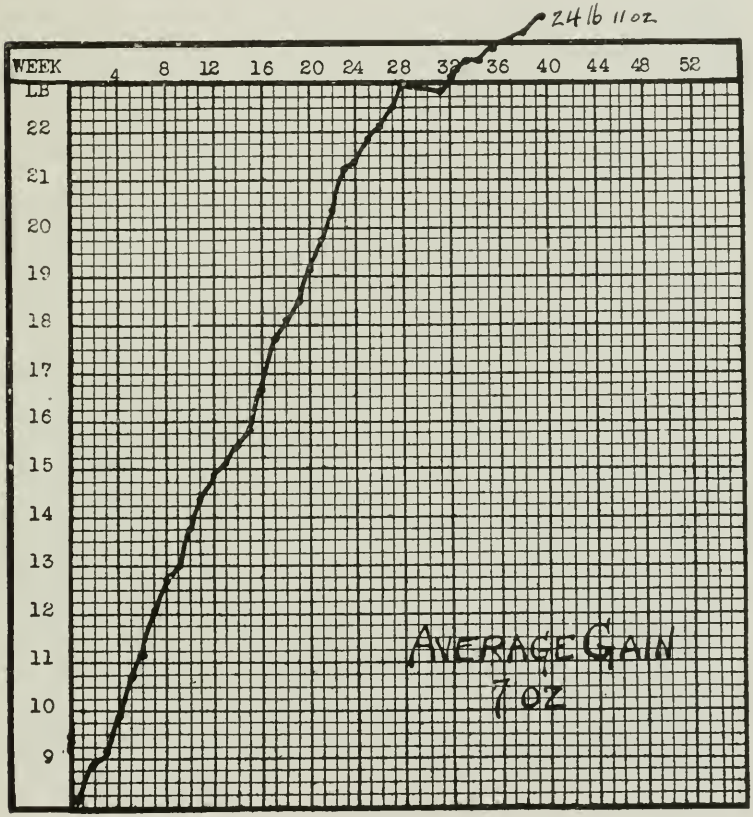

Figure 4.

from fish, and the milk disappeared. The baby was put upon a formula, and has been on various modifications of milk ever since. Is overweight, hard, and has gained well. Has never been ill, except during its thirtieth week, when it had a very bad infectious catarrhal cold accompanied by some temperature, loss of appetite and a good deal of cough. Now has cereal jelly added to formula and takes four feedings of 13 ounces each.

No. 4.

Formula	1	2	3	4	5	6	7	8	9
Fat percentage	1.60	2.3	1.8	1.7	2.+	....	....	3.3	....
Proteid percentage	1.40	1.60	1.60	1.60	1.6—	....	....	3.—	....
Amount in ounces	20	35	48	57	62	52	....	52	....

CASE 5.—R. N. Weighed 6 pounds, 12 ounces at birth. Was brought to us when eight weeks old with the statement that the breast milk did not agree with it, and that it had been on malted milk. Mother thinks has possibly gained, but

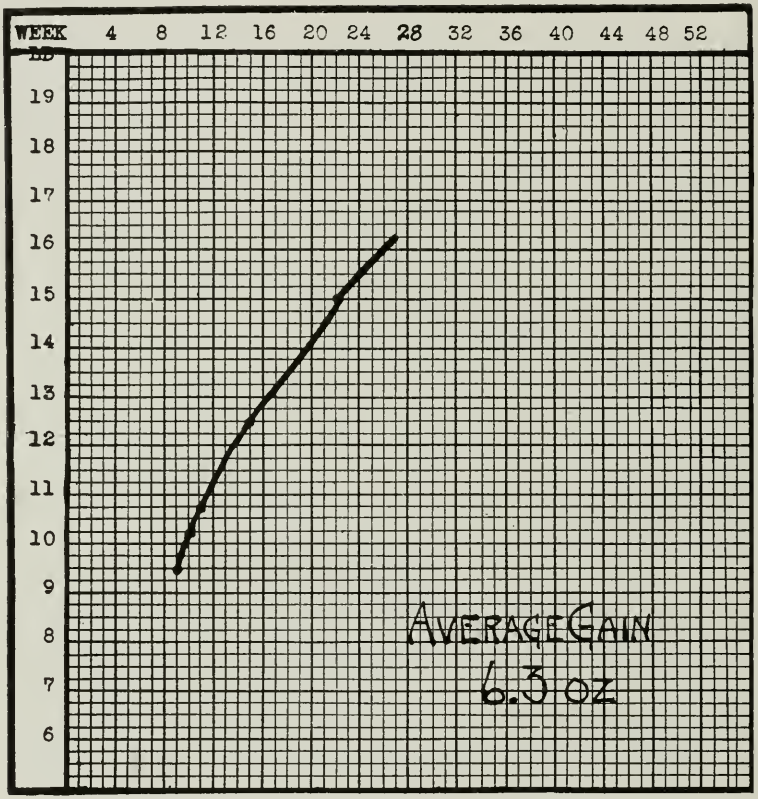

Figure 5.

probably not. Put upon a modified milk formula during its ninth week. Has gained, has been uninterruptedly good, and has been perfectly well during the whole time.

No. 5.

Formula	1	2	3	4	5	6
Fat percentage	2.—	2.0	2.4	2.66	2.56	2.56
Proteid percentage	1.42	1.64	1.75	1.75	1.82	1.96
Amount in ounces	32	32	40	42	50	50

CASE 6.—J. E. G. Was brought to us when six weeks old. Was breast fed for a week or two, then put on condensed milk for a short time, and of late has been on an extremely indefinite modification of indefinite milk. Having been put on a proper formula, immediately began to gain, and this gain has been continuous. You will note that the fifth and sixth formulas had below 2 per cent. of butter fat, as the child seemed to have too frequent bowel movements. Baby's general condition most excellent, flesh hardening well, skin very attractively wholesome.

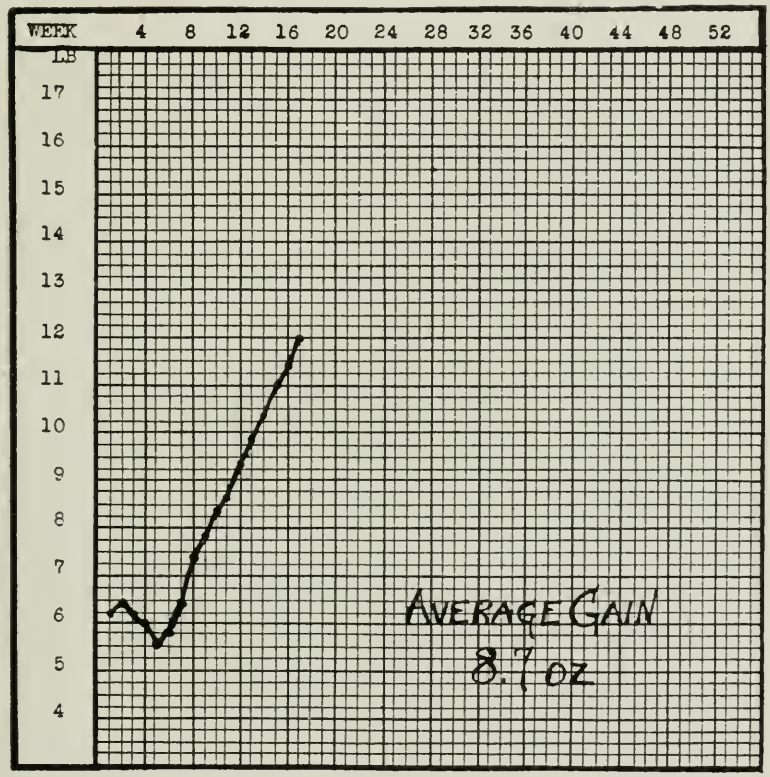

Figure 6.

No. 6.

Formula	1	2	3	4	5	6	7	8
Fat percentage	2.	2.+	2.+	2.3	1.9	1.8	2.	2.3
Proteid percentage	1.31	1.35	1.35	1.50	1.58	1.55	1.75	1.87
Amount in ounces	24	31	39	42	42	54	56	56

CASE 7.—M. M. S. Breast-milk supply lasted a very short time, and within a couple of weeks after birth was put on modified milk. Gained rather steadily, although not quite so evenly as some children. Any excess in fat seemed to cause

child to spit up a good deal. Every time child was about to erupt teeth had some catarrhal disturbance of mucous membranes, and did not gain quite as rapidly as usual. At present is well up to weight, exceedingly strong and well and very vigorous.

No. 7.

Formula	1	2	3	4	5	6	7	8	9
Fat percentage ..	2.3	2.	2.+	2.7	2.66	3.2	3.5	3.0	....
Proteid percentage	1.25	1.40	1.75	1.75	2.10	2.21	2.93	3.1	....
Amount in ounces	28	40	46	50	60	60	49	44	....

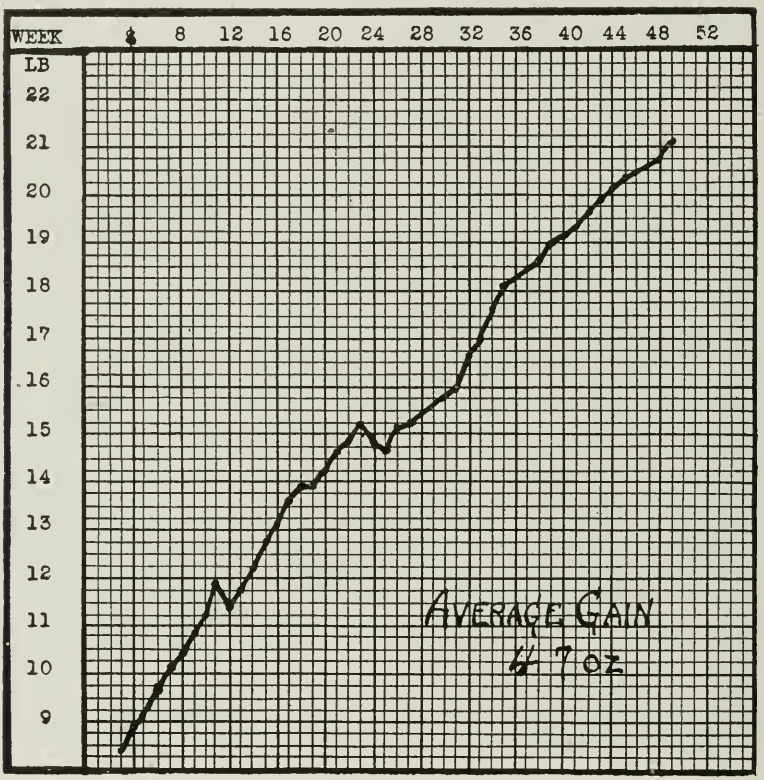

Figure 7.

CASE 8.—This child was brought to us when three months old. Although breast-fed was losing weight rapidly. Had not been fed at all regularly. Whey was given in addition to the breast feeding for a while, but soon, because of the failure of the breast milk, the baby was put on a formula. Began to gain fairly well, and with a few interruptions, which were due to an occasional cold, and once to the parents giving a formula of their own to the child, has gained with increased rapidity. Instead of milk sugar the child has had malted milk since

having formula, as it had been given malted milk in addition to the breast in its early days. It has now a good color, is strong, very active, and is rapidly approaching the normal line of gain. This case has been particularly interesting because of the very feeble condition the child was in, and because of the strenuous methods necessary to have the child treated with machine-like regularity. The initial appearance of the child was shocking in the extreme, its emaciation was great and its color was very poor. In fact, its condition was such as to preclude the probability of a favorable prognosis. It was a case of try and try hard.

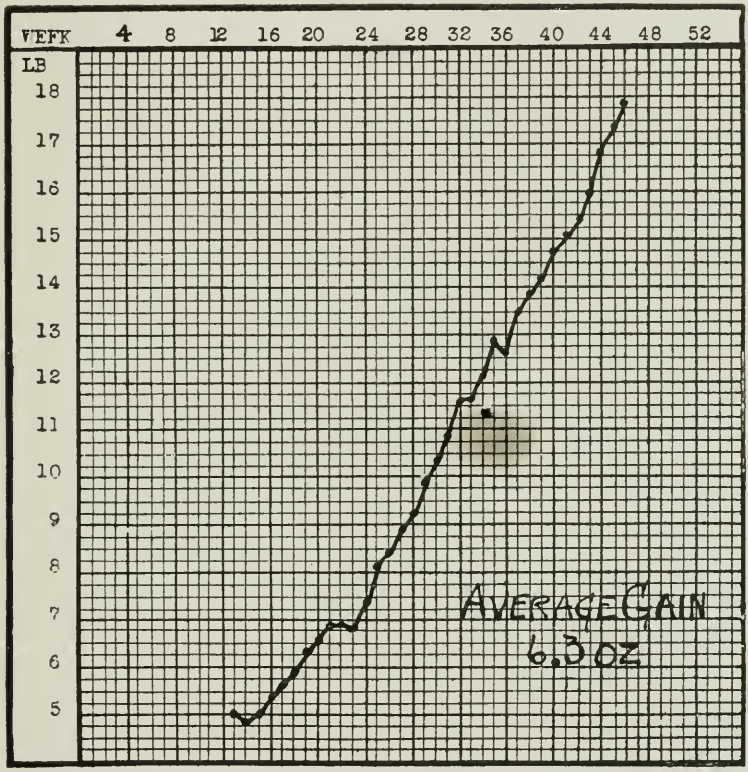

Figure 8.

No. 8.

Formula	1	2	3	4	5	6
Fat percentage	0.9	1.27	2.—	2.+	2.56	2.56
Proteid percentage	1.16	1.38	1.75	1.75	1.96	2.24
Amount in ounces	36	38	42	48	50	50

In the days of my house service at the Children's Hospital of Boston, we used to write formulas of fat 3:50 to 4:50; proteid 1 to 1:25 or 1:31 per cent., and give that to ordinary, average, very young babies, and

"get away with it," too. Fats in almost any amounts were then considered easy of digestion, and our bugbear was called "proteid" or "curd." In those days we had unmentionable milk, and for safety's sake we must needs sterilize every drop. We all, I think, believe that cooking milk alters the physical condition of the proteid content, rendering it less easy of digestion, and therein, I believe, lay our old-time difficulty with the administration of really sufficient proteid to insure the proper balance of growth.

As Rotch, of Boston, and Coit, of Newark, worked for better milk—cleaner milk—for milk that would not need sterilization to make and keep it useful; by so much as success crowned their efforts did we find that we could get along with pasteurized milk, and that, because of the lesser heat used, the proteids were better digested and more easily assimilated. When, later, certified milk or Walker-Gordon milk could be obtained, and the use of raw milk could be safely entered upon, we found that much higher percentages of proteid could be used profitably, and this series of cases gives, we think, a proof not only of this, but also a hint as to the cause of some of our old-time troubles among artificially-fed infants.

Babies grew fat and gained weight, but their progress was not, as a rule, of uninterrupted good health. Every now and again we were called to see a baby who was constipated, vomiting, full of gas, feverish; one whose bowels were very hard to clean out; one who, when the bowels were once started, had a number of indescribably filthy stools. Often these stools were black in color from the changes in the fats due to long retention in the bowel, and it is not surprising that the toxins so generated caused a rather stubborn and rather long-continued reaction.

Not one of the babies whose charts we show here has had any such attack, nor has any child in our practice who has been fed in this manner, i. e., low fats and comparatively high proteids. We dwell on this point, because it has seemed to have given us such uniformly good results, yet we do not in any way mean to intimate that there are not individual children who will do better upon higher percentages of fat and lower percentages of proteid. Each child should be considered, not as one of a class or group, but as a unit, and its food should be so designed (if we can so use the word) as to supply to the fullest extent its individual needs. Perhaps the charts have made plain the fact that each child has been allowed all the food it could take and take care of. No child under our care has ever been limited in the amount of its food by any preconceived

notion, based on any set of tables, of just how much a baby of its age or weight should hold. The "Progressive-Series-Feeding-Tables" idea, analogous to the composite photograph idea, should not be entertained by the real pediatrician. Babies are units, influenced by heredity and environment, and our most important task is to find out just what, and just how much, is most suitable for the given child. We are not necessarily striving to raise fat babies, but those that will be, and will remain, thoroughly well; who will have a consistent, normal growth and the greatest resistance.

To recapitulate:

1. A large number of babies thrive well on low fats and comparatively high proteids.

2. Their digestion and assimilation seems to be more than usually efficient.

3. Their freedom from gastro-intestinal disturbances is remarkable.

4. Their growth quite uniformly satisfactory.

5. Children should have in quantity all the food they can take and take care of.

6. Each child should be considered as a unit, and should be treated as such.

7. The best obtainable milk, most carefully handled, is none too good for the little people.

THE CODE OF STANDARDS OF THE AMERICAN ASSOCIATION OF MEDICAL MILK COMMISSIONS

HENRY L. COIT, M.D.
NEWARK, N. J.

Soon after the organization of the American Association of Medical Milk Commissions in 1906, which is a federation of Medical Society Milk Commissions, the chief objects of which are to extend the pure milk movement and to standardize clinical milk and milk for infant feeding, it became apparent that there was a great lack of uniformity in the quality, purity and safety of the product resulting from the activity of these commissions.

Attempts were made from year to year to adopt methods, regulations and standards for the guidance of these Commissions, of which there have come to be a large number in this country. These standards related to the hygienic, chemical, biological, veterinary and safety features of the plan to obtain clinically clean milk, but were not assembled in a comprehensive code embodying all that was best in methods employed by the leading Commissions and taught by the best authorities.

At the annual meeting held in Philadelphia in 1911, a committee composed of Assistant Surgeon-General John W. Kerr, Dr. S. McC. Hamill and the writer, was appointed to prepare a code of working methods and regulations, including definite standards of purity, quality and safety for certified milk, which should become the standards of the Association and a guide for all Commissions, so that certified milk shall be the same and equally reliable in all places, whether produced in Berkeley, Cal., or Boston, Mass.

The committee carefully studied all literature relating to the subject, issued a questionnaire to all known commissions throughout the world, of which there were nearly seventy, sifted the replies to sixty-nine questions from forty-four Commissions, and rendered its report to the sixth annual meeting held at Louisville, May 1, 1912. The report was adopted as the national code of standards for the production of certified milk.

It defines the produce, the functions and objects of the Medical Milk Commission; prescribes in detail the appointment and organization of the Medical Milk Commission; outlines the duties of the Commission,

the selection of the experts for the four lines of investigation and control required by the system.

Dairy Hygiene.—It establishes definite standards of dairy hygiene as to pastures, surroundings, location and construction of buildings and stables, drinking and feeding troughs, stanchions, ventilation, windows, exclusion of flies, exclusion of animals from herd, bedding, cleaning stables and disposal of waste; cleaning cows, clipping, cleaning udders, foods, feeding, exercise, washing of hands, milking clothes, things to be avoided by milkers, fore-milk, milk and calving period, bloody and stringy milk, grouping of herd, employees other than milkers, straining and strainers, dairy building, temperature of milk, sealing of bottles, cleaning and sterilization of bottles, utensils, water supply, privies in relation to the water supply, toilet rooms, transportation, thirty hours being maximum age of certified milk when delivered; veterinary supervision, tuberculin test, disposition of reactors, disinfection of stables and exercising yards; identification of cows, records of tests as to dates and results; retesting, disposition of cows sick with diseases other than tuberculosis, notification of veterinary inspector, emaciated cows and their removal.

Bacteriological Standards.—Bacterial counts, numerical standard of less than 10,000 bacteria per cubic centimeter when delivered, weekly counts being made, and daily when in excess; if the normal is not restored in ten days, certificate to be suspended; collection of samples for examination, interval between milking and plating, plating technique, controls and duration of incubation, the media, the preparation of media and methods are recommended, giving details to guide the bacteriologist employed by the Commission, determination of taste and odor of the milk at 100 F., the counts and records of bacteriological tests.

Chemical Standards and Methods.—Required findings to be reported by the chemist, method of obtaining samples, fat standard of 4 per cent., with a permissable range of variation of from 3.5 to 4.5 per cent.; fat standard for certified cream not less than 18 per cent., the content of both to be determined at least monthly; recommended methods are given in detail, including Babcock, Leffman-Beam and the Gerber. The protein standard for milk and cream is 3.5 per cent., with a permissible range of variation of from 3 to 4 per cent., determined by the Kjeldahl method; freedom of the milk from coloring matter and preservatives; tests for coloring matter, for formaldehyd, boric acid and borates, for

salicylic acid, salicylates and benzoic acid; tests for the detection of heated milk to be applied once each month; Storch's and Arnold's are given in detail; the microscopic test for heated milk of Frost and Ravenel is given; the specific gravity of 10.29 to 10.34 is required and methods of determining it are given.

The Methods and Regulations for the Medical Examination of Employes, their Health and Personal Hygiene.—An attending dairy physician is required, designated by the Commission, responsible to and reporting periodically to it; requirements for the physical examination of the workers on the dairy premises made periodically, and before new employees shall be brought to the plant; the examination and requirements having reference to recent vaccination, possible affections of the throat, tuberculosis, venereal disease, conjunctivitis, diarrhea, dysentery, typhoid fever or a typhoid carrier, disease of the respiratory tract, suppurative process, infectious skin eruption, any disease of an infectious or contagious nature or any person who has recently been associated with children sick of contagious disease; personal cleanliness of employees and, when housed on premises, proper habits and supervision of their living rooms, sleeping rooms, beds and bathing facilities are enjoined. When ill and resident on the dairy premises, a quarantine building is recommended, and its suitable construction is given in detail. The method of quarantine and isolation from the dairy of sick employees is given, with details for the taking of cultures of suspects and making reports to the Commission, with proper course for its officers pending ultimate consideration and action. Methods are recommended for safeguarding the milk while exposed to possible infection, by notification of facts, and efficient sterilization of the milk during the period of incubation for the disease in question. Methods are also recommended for the disinfection of the plant. Following a periodical medical inspection of employees, a monthly report is required to be filed with the secretary of the Commission by the attending physician on the same recurring date and upon a recommended schedule blank provided by the commission for this purpose, and designed to furnish information that will enable the commission to guarantee the health and safety of all the employees.

The Code of Standards is now in press and it will be published in a few days by the Surgeon-General of the United States.[1]

277 Mt. Prospect Avenue.

1. Public Health Rep., U. S. Pub. Health Service, June 14, 1912.

INDEX

TO THE

TRANSACTIONS

OF THE

AMERICAN PEDIATRIC SOCIETY

VOLUMES XV TO XXIV INCLUSIVE

Committee:

ROWLAND G. FREEMAN, M.D.
L. EMMETT HOLT, M.D.
LINNÆUS E. LA FÉTRA, M.D.

THE AMERICAN PEDIATRIC SOCIETY

HISTORICAL TABLE

YEARS.	PRESIDENTS.	PLACES OF MEETING.	PRESIDENTIAL ADDRESSES
1903	J. P. Crozer Griffith	Washington.	A Review of the Work of The American Pediatric Society.
1904	Augustus Caillé	Detroit.	The Influence of The American Pediatric Society in Promoting the Welfare of American Children.
1905	Charles Goodwin Jennings	Lake George.	The Medical Supervision of Schools and the Progress of School Hygiene.
1906	Abraham Jacobi.	Atlantic City.	The Tonsil as a Portal of Microbic and Toxic Invasion.
1907	B. K. Rachford.	Washington.	Pseudomasturbation in Infants.
1908	Charles Gilmore Kerley.	Delaware Water Gap.	Public School Education.
1909	Charles P. Putnam.	Lenox, Mass.	Medical Work in the Charitable Institutions of Boston.
1910	David L. Edsall.	Washington.	Pediatrics in America.
1911	Henry Dwight Chapin.	Lake Mohonk.	The Fundamental Principles of Pediatrics.
1912	Walter Lester Carr.	Hot Springs, Virginia.	The Relation of The American Pediatric Society to the Reduction of Mortality in Infancy and Childhood.

INDEX BY AUTHORS

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American Pediatric Society
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